~~10/513699~~ 10/561,101

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TERMINAL (ENTER 1, 2, 3, OR 7):2

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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JUL 02	LMEDLINE coverage updated
NEWS	3	JUL 02	SCISEARCH enhanced with complete author names
NEWS	4	JUL 02	CHEMCATS accession numbers revised
NEWS	5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS	6	JUL 16	CAplus enhanced with French and German abstracts
NEWS	7	JUL 18	CA/CAplus patent coverage enhanced
NEWS	8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS	9	JUL 30	USGENE now available on STN
NEWS	10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	11	AUG 06	BEILSTEIN updated with new compounds
NEWS	12	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	13	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS	14	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS	15	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	16	AUG 27	USPATOLD now available on STN
NEWS	17	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	18	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	19	SEP 13	FORIS renamed to SOFIS
NEWS	20	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	21	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS	22	SEP 17	CAplus coverage extended to include traditional medicine patents

NEWS EXPRESS 05 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 05 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:47:08 ON 18 SEP 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 15:47:13 ON 18 SEP 2007
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STRUCTURE FILE UPDATES: 17 SEP 2007 HIGHEST RN 947369-26-8
DICTIONARY FILE UPDATES: 17 SEP 2007 HIGHEST RN 947369-26-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

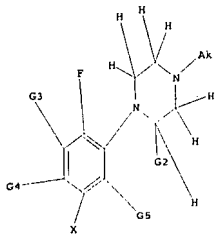
=>
Uploading C:\Program Files\Stnexp\Queries\10561101claim79.str

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

<12/04/2007> Erich Leese

10/513699



G1 C,H,Ak

G2 X,Ak,CF2,CF3

G3 X,CN

G4 C,O,Ak,CF3,X

G5 X,Me,CH2,CH,Et

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 15:48:01 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 8971 TO ITERATE

100.0% PROCESSED 8971 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L2 0 SEA SSS FUL L1

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	182.00	182.21

FILE 'REGISTRY' ENTERED AT 16:01:11 ON 18 SEP 2007
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DICTIONARY FILE UPDATES: 17 SEP 2007 HIGHEST RN 947369-26-8

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

<12/04/2007> Erich Leese

10/513699

Please note that search-term pricing does apply when conducting SmartSELECT searches.

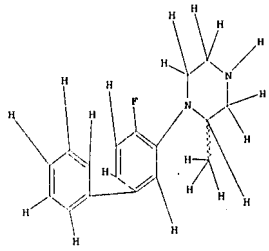
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10561101stereounspecific.str

L3 STRUCTURE UPLOADED

=> d l3
L3 HAS NO ANSWERS
L3 STR



G1 C,H,Ak

G2 X,Ak,CF2,CF3

G3 X,CN

G4 C,O,Ak,CF3,X

G5 X,Me,CH2,CH,Et

Structure attributes must be viewed using STN Express query preparation.

=> s l3 full
FULL SEARCH INITIATED 16:01:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 416 TO ITERATE

100.0% PROCESSED 416 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

<12/04/2007> Erich Leese

L4 4 SEA SSS FUL L3

=> file caplus
COST IN U.S. DOLLARS — SINCE FILE ENTRY: 172.10 — TOTAL SESSION: 354.31

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 16:01:46 ON 18 SEP 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 18 Sep 2007 VOL 147 ISS 13
FILE LAST UPDATED: 17 Sep 2007 (20070917/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l4 full
L5 1 L4

=> d ibib abs hitstr

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:158653 CAPLUS
DOCUMENT NUMBER: 142:261560
TITLE: Preparation of N-phenyl-piperazine derivatives and methods of prophylaxis or treatment of 5-HT2C receptor associated diseases
INVENTOR(S): Smith, Brian; Tsai, James; Chen, Rita
PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

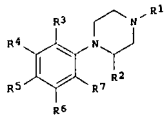
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016902	A1	20050224	WO 2004-US19540	20040617

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004265243	A1	20050224	AU 2004-265243	20040617
CA 2529750	A1	20050224	CA 2004-2529750	20040617
EP 1644347	A1	20060412	EP 2004-776755	20040617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1809545	A	20060726	CN 2004-80017001	20040617
BR 2004011661	A	20060829	BR 2004-11661	20040617
JP 2007523861	T	20070823	JP 2006-517403	20040617
MX 2005PA13365	A	20060405	MX 2005-PA13365	20051208
IN 2006KN00115	A	20070622	IN 2006-KN115	20060113
US 2007179155	A1	20070802	US 2006-561101	20060526
PRIORITY APPLN. INFO.:			US 2003-480045P	P 20030620
			WO 2004-US19540	W 20040617

OTHER SOURCE(S): CASREACT 142:261560; MARPAT 142:261560
GI



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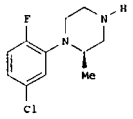


II

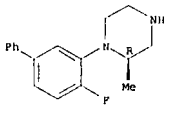
AB Title compds. I [wherein R1 = H, alkyl; R2 = alk(en)yl, haloalkyl; R3, R4, R5, R6, R7 = independently H, acyl, acyloxy, acylthioxy, alk(en)yl, halo/carbo/alkoxy, alkylcarboxamido, halo, OH, SH, Ph, halo/alkylsulfinyl, alkylsulfonamido, halo/alkylsulfonyl, halo/alkylthio, NH2, di/alkylamino, CN, haloalkyl; and their pharmaceutically acceptable salts, solvates or hydrates; with the proviso that certain compds. are excluded] were prepared as 5-HT2C receptor modulators, in particular agonists. Thus, II•xHCl was prepared by Pd-coupling of 2-Bromo-4-chloro-1-fluorobenzene with

4-(tert-butoxycarbonyl)-(R)-2-methylpiperazine. Intracellular IP3 accumulation assay (EC50 = 8.0 nM against the 5-HT2C receptor) and inhibition of food intake in food-deprived rats (see chart) were used to test the bioactivity of II. Certain compds. are selective for the 5-HT2C receptor compared to the 5-HT2A and 5-HT2B receptors; for example II has an EC50 value of 529 nM against the 5-HT2A receptor and is essentially inactive against the -5HT2B receptor. I are useful for the prophylaxis or treatment of 5-HT2C receptor associated diseases or disorders, such as, obesity, Alzheimer Disease, erectile dysfunction and related disorders.

IT 845741-28-8P, (R)-1-(4-Fluorobiphenyl-3-yl)-2-methylpiperazine hydrochloride 845741-29-9P, (S)-1-(4-Fluorobiphenyl-3-yl)-2-methylpiperazine hydrochloride 845742-44-1P, (R)-1-(4-Fluorobiphenyl-3-yl)-2-methylpiperazine 845742-45-2P, (S)-1-(4-Fluorobiphenyl-3-yl)-2-methylpiperazine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-phenylpiperazines as 5-HTC receptor modulators)

RN 845741-28-8 CAPLUS
CN Piperazine, 1-(4-fluoro[1,1'-biphenyl]-3-yl)-2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

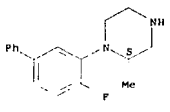
Absolute stereochemistry.



•x HCl

RN 845741-29-9 CAPLUS
CN Piperazine, 1-(4-fluoro[1,1'-biphenyl]-3-yl)-2-methyl-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

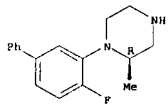
Absolute stereochemistry.



•x HCl

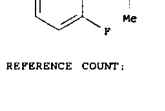
RN 845742-44-1 CAPLUS
CN Piperazine, 1-(4-fluoro[1,1'-biphenyl]-3-yl)-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 845742-45-2 CAPLUS
CN Piperazine, 1-(4-fluoro[1,1'-biphenyl]-3-yl)-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file reg
COST IN U.S. DOLLARS — SINCE FILE ENTRY: 9.97 — TOTAL SESSION: 364.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) — SINCE FILE ENTRY: -0.78 — TOTAL SESSION: -0.78
CA SUBSCRIBER PRICE

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STRUCTURE FILE UPDATES: 17 SEP 2007 HIGHEST RN 947369-26-8
DICTIONARY FILE UPDATES: 17 SEP 2007 HIGHEST RN 947369-26-8

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10561101final.str

L6 STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
L6 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l6 full
FULL SEARCH INITIATED 16:08:30 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 602595 TO ITERATE

100.0% PROCESSED 602595 ITERATIONS 1347 ANSWERS
SEARCH TIME: 00.00.05

L7 1347 SEA SSS FUL L6

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.10	536.38
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.78

FILE 'CAPLUS' ENTERED AT 16:08:40 ON 18 SEP 2007
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FILE COVERS 1907 - 18 Sep 2007 VOL 147 ISS 13
FILE LAST UPDATED: 17 Sep 2007 (20070917/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l7 full
L8 201 L7

=> s l8 and py<2003
22890048 PY<2003
L9 134 L8 AND PY<2003

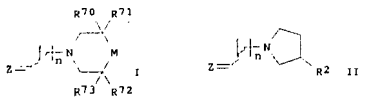
=> d ibib abs hitstr tot

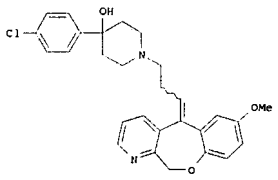
L9 ANSWER 1 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:284138 CAPLUS
DOCUMENT NUMBER: 142:355256
TITLE: Preparation of tricyclic-substituted piperidinols and analogs as chemokine receptor antagonists
INVENTOR(S): Luly, Jay R.; Nakasato, Yoshisuke; Ohshima, Etsuo; Harriman, Geraldine C. B.; Carson, Kenneth G.; Ghosh, Shomir; Elder, Amy M.; Mattia, Karen M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 194 pp., Cont.-in-part of U.S. Ser. No. 989,086, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005070549	A1	20050331	US 2004-487168	20041007
US 7186729	B2	20070306		
US 6613905	B1	20030902	US 1998-148823	19980904
US 6329385	B1	20011211	US 1999-235102	19990121 <--
US 2002119973	A1	20020829	US 1999-362837	19990728 <--
US 6509346	B2	20030121		
US 2002169155	A1	20021114	US 2001-989086	20011121 <--
WO 2003045942	A2	20030605	WO 2002-US36953	20021113
WO 2003045942	A3	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2007060592	A1	20070315	US 2006-595653	20061110
AU 2007200261	A1	20070208	AU 2007-200261	20070123
PRIORITY APPLN. INFO.:			US 1998-148823	A2 19980904
			US 1999-235102	A2 19990121

	US 1999-362837	A2 19990728
	US 2000-627886	B2 20000728
	US 2001-989086	B2 20011121
	WO 2002-US36953	W 20021113
	US 1998-10320	B2 19980121
	AU 2002-352772	A3 20021113
	US 2004-487168	A1 20041007

OTHER SOURCE(S): MARPAT 142:355256
GI





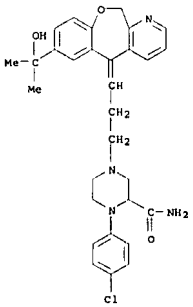
III

AB Therapeutically effective compds. I [Z = (un)substituted heterocyclic ring fused to one or more carbocyclic aromatic rings; n = 1-4; M = NR2, CR1R2; R1 = H, OH, N3, etc.; R2 = OH, halo, acyl, aryl, etc.; R70, R71 = H, OH, N3, etc.; R72, R73 = O, N2, halo, etc.] and II [Z, n are defined as above; R2 = OH, halo, acyl, aryl, etc.] were prepared for treatment of diseases associated with aberrant leukocyte recruitment and/or activation (no data). I and II displayed chemokine binding activities with IC50 values ranging from < 1 μM to < 1000 μM. Thus, the [(1]benzoxepino[2,3-b]pyridinylidene)propyl]piperidinol III was prepared in three steps by reaction of 5,11-dihydro-7-methoxy[1]benzoxepino[2,3-b]pyridin-5-one with cyclopropylmagnesium bromide in THF, followed by ring cleavage-dehydration-bromination with HBr, and addition of 4-(4-chlorophenyl)-4-hydroxypiperidine to the bromide in DMF. Major and minor isomers were separated The pharmaceutical compns. comprising the compound I or II is disclosed.

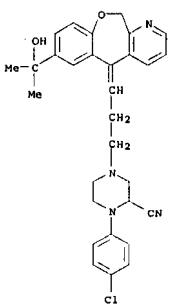
IT 849105-73-3P 849105-74-4P 849105-75-5P
849105-85-7P 849105-86-8P 849105-87-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tricyclic piperidinols and pyrrolidines as chemokine receptor antagonists for treatment of diseases associated with aberrant leukocyte recruitment and activation)

RN 849105-73-3 CAPLUS

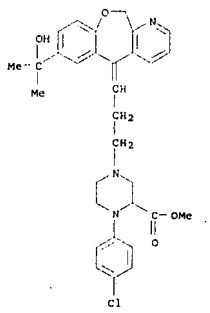
CN 2-Piperazinecarboxamide, 1-(4-chlorophenyl)-4-[3-[7-(1-hydroxy-1-methylethyl)[1]benzoxepino[3,4-b]pyridin-5(11H)-ylidene]propyl]- (9CI) (CA INDEX NAME)



RN 849105-74-4 CAPLUS
CN 2-Piperazinecarbonitrile, 1-(4-chlorophenyl)-4-[3-[7-(1-hydroxy-1-methylethyl)[1]benzoxepino[3,4-b]pyridin-5(11H)-ylidene]propyl]- (9CI) (CA INDEX NAME)

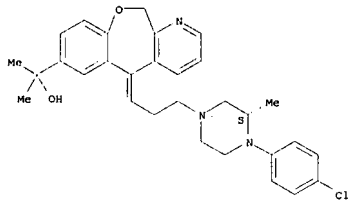


RN 849105-75-5 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-(4-chlorophenyl)-4-[3-[7-(1-hydroxy-1-methylethyl)[1]benzoxepino[3,4-b]pyridin-5(11H)-ylidene]propyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 849105-85-7 CAPLUS
CN [1]Benzoxepino[3,4-b]pyridine-7-methanol, 5-[3-[(3S)-4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propylidene]-5,11-dihydro- α,α-dimethyl- (9CI) (CA INDEX NAME)

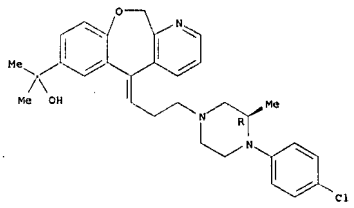
Absolute stereochemistry.
Double bond geometry unknown.



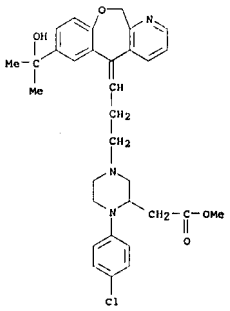
RN 849105-86-8 CAPLUS
CN [1]Benzoxepino[3,4-b]pyridine-7-methanol, 5-[3-[(3R)-4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propylidene]-5,11-dihydro- α,α-dimethyl-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



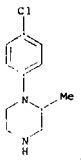
RN 849105-87-9 CAPLUS
CN 2-Piperazineacetic acid, 1-(4-chlorophenyl)-4-[3-[7-(1-hydroxy-1-methylethyl)[1]benzoxepino[3,4-b]pyridin-5(11H)-ylidene]propyl]-, methyl ester (9CI) (CA INDEX NAME)



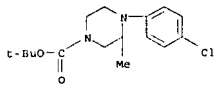
IT 55117-80-1P, 1-(4-Chlorophenyl)-2-methylpiperazine
849105-48-5P, 4-(4-Chlorophenyl)-3-methylpiperazine-1-carboxylic acid tert-butyl ester 849106-90-7P 849106-91-8P
849107-16-0P 849107-17-1P 849107-18-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of tricyclic piperidinols and pyrrolidines as chemokine receptor antagonists for treatment of diseases associated with aberrant leukocyte recruitment and activation)

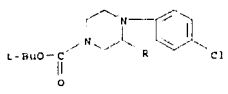
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



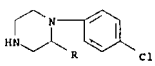
RN 849106-48-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(4-chlorophenyl)-3-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 849106-90-7 CAPLUS
CN 1,3-Piperazinedicarboxylic acid, 4-(4-chlorophenyl)-, 1-(1,1-dimethylethyl) 3-methyl ester (9CI) (CA INDEX NAME)

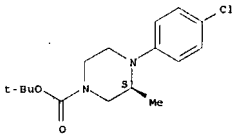


RN 849106-91-8 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-(4-chlorophenyl)-, methyl ester (9CI) (CA INDEX NAME)



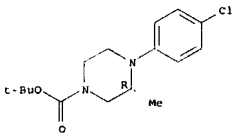
RN 849107-16-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(4-chlorophenyl)-3-methyl-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

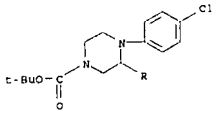


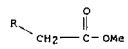
RN 849107-17-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(4-chlorophenyl)-3-methyl-, 1,1-dimethylethyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 849107-18-2 CAPLUS
CN 2-Piperazineacetic acid, 1-(4-chlorophenyl)-4-[(1,1-dimethylethoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)





REFERENCE COUNT: 151 THERE ARE 151 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:485162 CAPLUS
DOCUMENT NUMBER: 141:38534
TITLE: Preparation of aromatic sultone hydroxamic acid metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.; Carroll, Jeffrey N.; Decrescenzo, Gary A.; Fobian, Yvette M.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Li, Madeleine H.; Hockerman, Susan L.; Howard, Susan C.; Kolodziej, Steve A.; Mischke, Deborah A.; Rico, Joseph G.; Stehle, Nathan W.; Tollefson, Michael B.; Vernier, William F.; Villamil, Clara I.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S., 403 pp., Cont.-in-part of U.S. Ser. No. 311,837.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

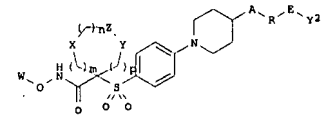
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6750228	B1	20040615	US 2000-570731	20000512
US 2001014688	A1	20010816	US 1998-191129	19981113 <--
US 2001039287	A1	20011108	US 1999-256948	19990224 <--
CA 2372934	A1	20001123	CA 2000-2372934	20000515 <--
WO 2000069821	A1	20001123	WO 2000-US6719	20000515 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1183239	A1	20020306	EP 2000-930088	20000515 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

HU 200201680	A2	20020928	HU 2002-1680	20000515 <--
BR 2000010562	A	20030610	BR 2000-10562	20000515
JP 2003520196	T	20030702	JP 2000-618238	20000515
AU 766792	B2	20031023	AU 2000-47970	20000515
NZ 515217	A	20040430	NZ 2000-515217	20000515
US 2002177588	A1	20021128	US 2001-954451	20010917 <--
US 6750233	B2	20040615		
ZA 2001009006	A	20021202	ZA 2001-9006	20011031 <--
NO 2001005543	A	20020110	NO 2001-5543	20011113 <--
MX 2001PA11569	A	20050620	MX 2001-PA11569	20011113
US 2003073718	A1	20030417	US 2001-989943	20011121
US 6683093	B2	20040127		
US 2004209914	A1	20041021	US 2003-730403	20031208
US 2004235818	A1	20041125	US 2003-747796	20031229

PRIORITY APPLN. INFO.:

US 1997-66007P	P	19971114
US 1998-95347P	P	19980804
US 1998-101080P	P	19980918
US 1999-256948	B2	19990224
US 1999-311837	A2	19990514
US 1998-95601P	P	19980806
US 1998-186410	B2	19981105
US 1998-191129	B2	19981113
US 2000-570731	A	20000512
WO 2000-US6719	W	20000515
US 2001-989943	A3	20011121

OTHER SOURCE(S): MARPAT 141:38534
GI



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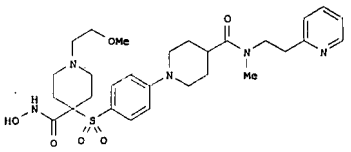


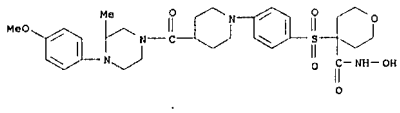
II

AB A treatment process is disclosed that comprises administering an effective amount of an aromatic sulfone hydroxamic acid I [W = H, cation, certain acyl or thioacyl groups; m, n, p = 0-2; (m+n+p) = 1 to 4; Z = (un)substituted NH; X, Y = (un)substituted CH2; A = bond, O, S, (un)substituted NH, COO, OCO,

CH:CH, C.tplbond.C, N:N, NHNH, NHCOO, (un)substituted CONH, NHCO, etc.; R = alkylene, arylene, heteroarylene, etc., with provisos; E = bond, CONH, NHCO, CO, SO2, NHSO2, SO2NH, S, etc.; Y2 = absent, H, alkyl, alkoxy, aryl, aryloxy, heteroaryl, etc.] to a host having a condition associated with pathol. matrix metalloprotease (MMP) activity. I exhibit excellent inhibitory activity of one or more MMP enzymes, such as MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibition of (at least) MMP-1 (biol. data given). Also disclosed are metalloprotease inhibitor compds. having such selective activities, processes for manufacture of such compds., and pharmaceutical compns. using such inhibitors. The compds. are potentially useful against a wide variety of conditions, notably as antiosteoarthritic, antiangiogenesis, and antitumor agents. Over 900 example compds. are listed, most with supporting phys. data, and many with synthetic details. E.g., a multi-step synthesis of the compound II.2HCl was given.

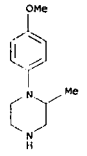
IT 308821-73-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aromatic sultone hydroxamic acids as metalloprotease inhibitors)

RN 308821-73-0 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[4-[[4-(4-methoxyphenyl)-1-methyl-1-piperazinyl]carbonyl]-1-piperidinyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



IT 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of aromatic sultone hydroxamic acids as metalloprotease inhibitors)

RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS

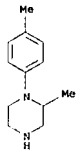
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:551964 CAPLUS
DOCUMENT NUMBER: 140:195578
TITLE: Customization of a commercially available prepare scale SFC system to provide enhanced capabilities
AUTHOR(S): Olson, Jeff; Pan, Jeff; Hochlowski, Jill; Searle, Philip; Blanchard, Dave
CORPORATE SOURCE: Abbot Laboratories, IL, USA
SOURCE: JALA (2002), 7(4), 69-74
CODEN: JALLFO; ISSN: 1535-5535
PUBLISHER: Association for Laboratory Automation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Preparative Scale Supercrit. Fluid Chromatog. is emerging as a powerful alternative to HPLC for the purification and separation of complex chemical reaction mixts. Advantages include greatly reduced solvent usage (and thus lower cost and environmental impact), higher throughput, and in some cases higher resolution. While there are com. available prepare SFC instruments, none currently offer all the features desired by many medicinal chemists engaged in the drug discovery process. These include: the ability to collect an unlimited number of fractions per sample with high recovery and negligible carryover, fully automated capacity to collect several hundred fractions, and the ability to collect fractions into the same disposable test tubes and racks which are already employed in HPLC. This article describes the customization of a preparatory scale SFC system purchased from Berger Instruments, Inc., Newark, DE. (a subsidiary Mettler-Toledo International, Inc., of Greifensee, Switzerland) in order to provide these capabilities.

IT 35947-11-6P, 1-(4-Methylphenyl)-2-methylpiperazine
RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(customization of a com. available prepare scale supercrit. fluid chromatog. (SFC) system to provide enhanced capabilities)

RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

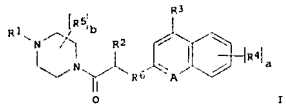
L9 ANSWER 4 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:946267 CAPLUS

DOCUMENT NUMBER: 138:24727
TITLE: Preparation of 2-[(piperazinocarbonylmethyl)aminocarbonyl]quinolines as platelet adenosine diphosphate receptor antagonists
INVENTOR(S): Bryant, Judi A.; Buckman, Brad O.; Islam, Imadul; Mohan, Raju; Morrissey, Michael M.; Wei, Guo Pin; Xu, Wei; Yuang, Shendong
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098856	A2	20021212	WO 2002-US17821	20020606 <--
WO 2002098856	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003060474	A1	20030327	US 2002-163742	20020605
US 6861424	B2	20050301		
AU 2002316191	A1	20021216	AU 2002-316191	20020606 <--
EP 1412349	A2	20040428	EP 2002-746471	20020606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004532886	T	20041028	JP 2003-501845	20020606
US 2005038037	A1	20050217	US 2004-947579	20040922
US 7026323	B2	20060411		
US 2005065163	A1	20050324	US 2004-947635	20040922
US 6995156	B2	20060207		
US 2006135532	A1	20060622	US 2006-347768	20060202
US 7176207	B2	20070213		

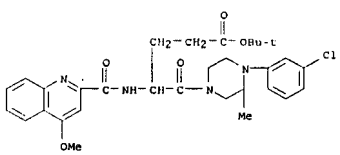
PRIORITY APPLN. INFO.: US 2001-296498P P 20010606
US 2002-163742 A 20020605
WO 2002-US17821 W 20020606
US 2004-947579 A3 20040922

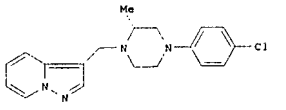
OTHER SOURCE(S): MARPAT 138:24727
GI



I

AB The title compds. [I; a, b = 1-4; A = CH, N; R1 = H, alkyl, aryl, etc.; R2 = H, alkyl, aryl, etc.; R3 = H, alkyl, OH, etc.; R4 = H, alkyl, alkoxy, etc.; R5 = H, alkyl, hydroxyalkyl, etc.; R6 = NR7CO, CONR7; R7 = H, alkyl, carboxyalkyl, alkoxycarbonylalkyl], useful as inhibitors of platelet aggregation and thrombus formation, were prepared and formulated. Thus, amidation of 7-methyl-4-hydroxy-2-carboxyquinoline with 4-ethoxycarbonyl-1-[1-amino-3-(1,1-dimethylethoxycarbonyl)propyl]carbonylpiperazine (preparation of both reactants given) afforded 68% I (R1 = CO2Et; R2 = tert-BuOCOCH2CH2; R3 = OH; R4 = 7-Me; R5 = H; R6 = NHCO; A = N). The compds. I demonstrated their ability to inhibit the binding of [33P]-2-methylthio-ADP binding to the human platelet ADP receptor and the rat platelet ADP receptor.
IT 478004-45-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-[(piperazinocarbonylmethyl)aminocarbonyl]quinolines as platelet ADP receptor antagonists)
RN 478004-45-4 CAPLUS
CN 1-Piperazinepentanoic acid, 4-(3-chlorophenyl)-γ-[[(4-methoxy-2-quinolinyl)carbonyl]amino]-3-methyl-δ-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

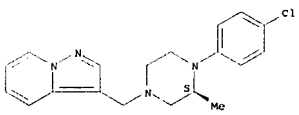




I

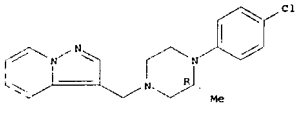
AB By employing yeast enzymes, natural amino acids and Jacobsen's catalyst as sources of chirality, pyrazolo[1,5-a]pyridine deriva. with central and planar chirality were prepared as analogs of the dopamine D4 receptor ligand FAUC 113. In vitro binding expts. displayed enhanced D2 and D3 affinity for both enantiomers of the [2.2]paracyclophane derivative The C-methylpiperazine (R)-I revealed excellent D4 selectivity.
IT 511255-13-3P 511255-27-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and activity of analogs of the dopamine D4 receptor ligand FAUC 113 with planar and central chirality)
RN 511255-13-3 CAPLUS
CN Pyrazolo[1,5-a]pyridine, 3-[[(3S)-4-(4-chlorophenyl)-3-methyl-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 511255-27-9 CAPLUS
CN Pyrazolo[1,5-a]pyridine, 3-[[(3R)-4-(4-chlorophenyl)-3-methyl-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

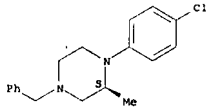


IT 511254-97-0P 511255-00-8P 511255-18-8P
511255-22-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and activity of analogs of the dopamine D4 receptor ligand FAUC

L9 ANSWER 5 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:862481 CAPLUS
DOCUMENT NUMBER: 138:304237
TITLE: Analogs of the dopamine D4 receptor ligand FAUC 113 with planar- and central-chirality
AUTHOR(S): Lober, Stefan; Ortner, Birgit; Bettinetti, Laura; Hubner, Harald; Gmeiner, Peter
CORPORATE SOURCE: Emil Fischer Center, Department of Medicinal Chemistry, Friedrich-Alexander University, Erlangen, D-91052, Germany
SOURCE: Tetrahedron: Asymmetry (2002), 13(21), 2303-2310
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:304237
GI

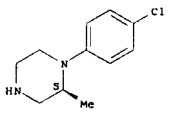
113 with planar and central chirality)
RN 511254-97-0 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



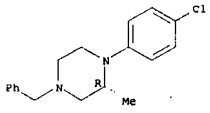
RN 511255-00-8 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



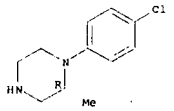
RN 511255-18-8 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 511255-22-4 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



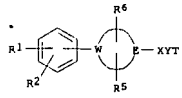
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:714060 CAPLUS
DOCUMENT NUMBER: 137:232677
TITLE: Preparation of heterocyclylphenyls for treatment of thromboembolic diseases and tumors
INVENTOR(S): Mederski, Werner; Cezanne, Bertram; Dorsch, Dieter; Tsaklakidis, Christos; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

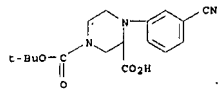
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10112768	A1	20020919	DE 2001-10112768	20010316 <--
CA 2440954	A1	20020926	CA 2002-2440954	20020227 <--
WO 2002074765	A1	20020926	WO 2002-EP2092	20020227 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002249246	A1	20021003	AU 2002-249246	20020227 <--
EP 1368341	A1	20031210	EP 2002-718165	20020227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200303539	A2	20040128	HU 2003-3539	20020227
CN 1496361	A	20040512	CN 2002-806536	20020227
JP 2004527514	T	20040909	JP 2002-573774	20020227
MX 2003PA08216	A	20040129	MX 2003-PA8216	20030911
US 2004082563	A1	20040429	US 2003-471768	20030916
ZA 2003008028	A	20050117	ZA 2003-8028	20031015

PRIORITY APPLN. INFO.: DE 2001-10112768 A 20010316
WO 2002-EP2092 W 20020227

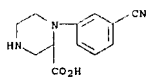
OTHER SOURCE(S): MARPAT 137:232677
GI



AB Title compds. [I; R1 = H, cyano, (substituted) C(:NH)NH2, CON(R3)2, [C(R4)2]nN(R3)2, etc.; R2, R5, R6 = H, halo, A, OR3, N(R3)2, NO2, cyano, [C(R4)2]nAr, [C(R4)2]nHet, [C(R4)2]ncycloalkyl, etc; R3 = H, A, [C(R4)2]nAr, [C(R4)2]nHet, [C(R4)2]ncycloalkyl; R4 = H, A; W = N, CR3; EW = 3-7 membered (substituted) (saturated) (benzo-, heterocyclyl-condensed) (hetero)cyclyl; X = [C(R4)2]nCONR3[C(R4)2]n, [C(R4)2]nNR3CO[C(R4)2]n, etc; Y = alkylene, cycloalkylene, heterocyclyldiyl, aryldiyl; T = (substituted) (bi)heterocyclyl; A = (branched) (O-, S-, CH:CH-interrupted) (fluorinated) C1-6 alkyl; Ar = (substituted) Ph, naphthyl, biphenyl; Het = (substituted) (aromatic) (bi)heterocyclyl; n = 0-2], were prepd as inhibitors of factor Xa and VIIa (no data). Thus, a mixture of 4-(tert-butoxycarbonyl)-1-(3-cyanophenyl)piperazine-2-carboxylic acid, 1-(4-aminophenyl)piperidin-2-one, N-(3-dimethylaminopropyl)-N-ethylcarbodiimide hydrochloride, and hydroxybenzotriazole hydrate in DMF was stirred with 4-methylmorpholine for 18 h at room temperature to give 4-(3-cyanophenyl)-3-[4-(2-oxopiperidin-1-yl)phenylcarbamoyl]piperazine-1-carboxylic acid tert-Bu ester which was stirred with DMSO, K2CO3, and H2O2 in MeOH for 2 h at room temperature to give (3-carbamoylphenyl)-3-[4-(2-oxopiperidin-yl)phenylcarbamoyl]piperazine-1-carboxylic acid tert-Bu ester. The latter was treated with HCl in dioxane for 1 h to give 1-[(3-carbamoylphenyl)-piperazin-2-yl]-N-[4-(2-oxopiperidin-1-yl)phenyl]amide.
IT 459132-99-1P 459133-00-7P 459133-05-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclylphenyls for treatment of thromboembolic diseases and tumors)
RN 459132-99-1 CAPLUS
CN 1,3-Piperazinedicarboxylic acid, 4-(3-cyanophenyl)-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

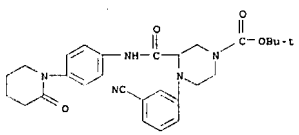


RN 459133-00-7 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-(3-cyanophenyl)-, monopotassium salt (9CI) (CA INDEX NAME)



● K

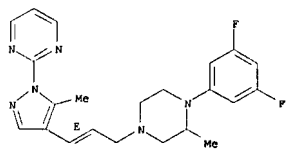
RN 459133-05-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(3-cyanophenyl)-3-[[[4-(2-oxo-1-piperidinyl)phenyl]amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 7 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:469715 CAPLUS
DOCUMENT NUMBER: 137:384813
TITLE: Synthesis and antitumor activity of novel pyrimidinyl pyrazole derivatives. II. Optimization of the phenylpiperazine moiety of 1-[5-methyl-1-(2-pyrimidinyl)-4-pyrazolyl]-3-phenylpiperazinyl-1-trans-propenes
AUTHOR(S): Naito, Hiroyuki; Ohsuki, Satoru; Sugimori, Masamichi; Atsumi, Ryo; Minami, Megumi; Nakamura, Yoshihide; Ishii, Mineko; Hirotani, Kenji; Kumazawa, Eiji; Ejima, Akio
CORPORATE SOURCE: Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co., Ltd., Tokyo, 134-8630, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2002), 50(4), 453-462
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:384813
AB A series of novel 3-substituted-1-[5-methyl-1-(2-pyrimidinyl)-4-pyrazolyl]-1-trans-propenes in order to improve the in vitro and in vivo activity of our prototype 3-[4-(3-chlorophenyl)-1-piperazinyl]-1-[5-methyl-1-(2-pyrimidinyl)-4-pyrazolyl]-1-trans-propene (I) were synthesized and evaluated by assays of growth inhibition against several tumor cell lines in vitro and antitumor activity against some tumor models when dosed both i.p. and orally in vivo. The 3,5-difluorophenyl and 3,5-dichlorophenyl

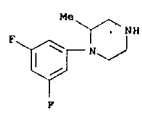
analogs of I showed significantly more potent cytotoxicity than I in vitro and potent antitumor activities without causing decrease of body temperature related to side effects.
IT 475653-33-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and optimization of phenylpiperazine moiety of novel pyrimidinyl pyrazole derivs. in relation to their antitumor activities)
RN 475653-33-9 CAPLUS
CN Pyrimidine, 2-[4-[(1E)-3-[4-(3,5-difluorophenyl)-3-methyl-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● HCl

IT 475653-31-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and optimization of phenylpiperazine moiety of novel pyrimidinyl pyrazole derivs. in relation to their antitumor activities)
RN 475653-31-7 CAPLUS
CN Piperazine, 1-(3,5-difluorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:293657 CAPLUS
DOCUMENT NUMBER: 136:310065
TITLE: Preparation of substituted piperazine-condensed

morphinoid derivatives as selective δ-opioid agonists and antagonists for treatment of conditions involving δ-opioid receptors

INVENTOR(S): Dondio, Giulio; Gagliardi, Stefania; Graziani, Davide; Raveglia, Luca Francesco

PATENT ASSIGNEE(S): Glaxosmithkline S.P.A., Italy

SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

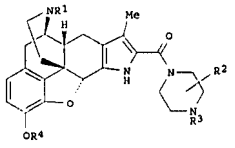
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030935	A1	20020418	WO 2001-EP11558	20011005 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002024772	A5	20020422	AU 2002-24772	20011005 <--
EP 1326868	A1	20030716	EP 2001-986688	20011005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511486	T	20040415	JP 2002-534321	20011005
US 2004067959	A1	20040408	US 2003-398313	20031003

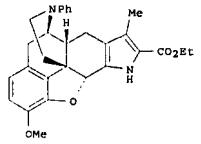
PRIORITY APPLN. INFO.: GB 2000-25056 A 20001012
WO 2001-EP11558 W 20011005

OTHER SOURCE(S): MARPAT 136:310065

GI



I



II

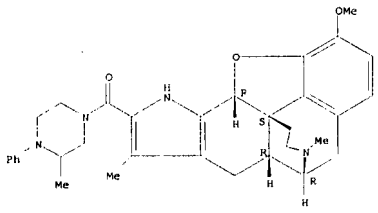
AB Substituted piperazine-condensed morphinoid derivs. I (R1 = H or alkyl; R2 = H or one or more alkyl groups; R3 is R or RX-; wherein R is H or optionally substituted alkyl, aryl, arylalkyl, cycloalkyl or heterocyclyl and X is a linking group; and R4 = H or alkyl; when R4 = Me and R3 = Me or hydroxyethyl then R2 is not H) were prepared as selective δ-opioid agonists and antagonists. Thus hydrocodeinone was treated with 3-oxo-2-(phenylhydrazono)butyric acid Et ester to give II. II was converted to the acid chloride which reacted with 4-chlorophenylpiperazine HCl to give derivative I (R1 = R4 = Me, R2 = H, R3 = 4-ClC6H4). The activity of the prepared compds. as selective δ-opioid receptor ligands was evaluated in radioligand binding assays using cloned human δ, μ and κ opioid receptors expressed in HEK cells (no data). The most potent compds. showed affinities for the δ receptor ranging from 0.3 to 10 nM with delta selectivity ranging from 15 to 400 times in respect to the other opioid receptor types (no data).

IT 409305-16-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted piperazine-condensed morphinoid derivs. as selective δ-opioid agonists and antagonists)

RN 409305-16-4 CAPLUS

CN Piperazine, 2-methyl-4-[[(4bS,8R,8aR,12bR)-5,6,7,8,8a,9,12,12b-octahydro-1-methoxy-7,10-dimethyl-4,8-methanobenzofuro[3,2-e]pyrrolo[2,3-g]isoquinolin-11-yl]carbonyl]-1-phenyl- (9CI) (CA INDEX NAME)

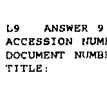
Absolute stereochemistry.



IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted piperazine-condensed morphinoid derivs. as selective δ-opioid agonists and antagonists)

RN 2946-76-1 CAPLUS

CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:142707 CAPLUS

DOCUMENT NUMBER: 136:200181

TITLE: Substituted and/or fused pyrazoles, particularly piperazinylpropyl-substituted pyrazolopyridines, useful as cathepsin S inhibitors, and their pharmaceutical compositions and use as immunosuppressants

INVENTOR(S): Breitenbucher, J. Guy; Cai, Hui; Edwards, James P.; Grice, Cheryl A.; Gustin, Darin J.; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Tays, Kevin L.; Wei, Jianmei

PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014314	A2	20020221	WO 2001-US25289	20010810 <--
WO 2002014314	A3	20020606		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2419540	A1	20020221	CA 2001-2419540	20010810 <--
AU 200181255	A	20020225	AU 2001-81255	20010810 <--
US 2002040020	A1	20020404	US 2001-928122	20010810 <--
EP 1309591	A2	20030514	EP 2001-959731	20010810
EP 1309591	B1	20070124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004512272	T	20040422	JP 2002-519454	20010810
NZ 524193	A	20041224	NZ 2001-524193	20010810
RU 2286343	C2	20061027	RU 2003-107018	20010810
AT 352552	T	20070215	AT 2001-959731	20010810
MX 2003PA01421	A	20040126	MX 2003-PA1421	20030214
IN 2003KN00189	A	20050311	IN 2003-KN189	20030214
ZA 2003002052	A	20040623	ZA 2003-2052	20030313
US 2007004754	A1	20070104	US 2006-517040	20060907
US 2007004755	A1	20070104	US 2006-517145	20060907
US 2007004738	A1	20070104	US 2006-517171	20060907
US 2007004747	A1	20070104	US 2006-517518	20060907
US 2007010530	A1	20070111	US 2006-517062	20060907
US 2007021437	A1	20070125	US 2006-517212	20060907

PRIORITY APPLN. INFO.: US 2000-225138P P 20000814
US 2001-928122 A 20010810
WO 2001-US25289 W 20010810

OTHER SOURCE(S): MARPAT 136:200181

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

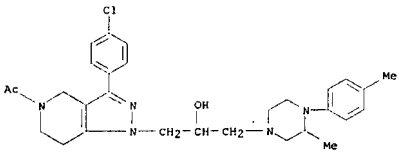
AB Substituted pyrazoles I, methods of manufacturing them, compns. containing them, and
methods of using them to treat, for example, autoimmune diseases mediated by cathepsin S, are described [R1 = H, N3, halo, alkoxy, OH, alkyl, alkenyl, cyano, NO2, (un)substituted NH2, acyl, etc.; R2 = H, halo, alkoxy, alkyl, alkenyl, haloalkyl, cyano, or (un)substituted NH2; or R1R2 = atoms to form (un)substituted (un)saturated (non)aromatic 5- to 7-membered carbo- or heterocyclic ring; R3, R4 = H, alkyl; R5, R6 = H, alkyl, alkenyl, alkoxy, alkylthio, halo, or 4- to 7-membered carbo- or heterocyclyl; or R5R6 = atoms to form (un)substituted (un)saturated (non)aromatic
5- to 7-membered carbo- or heterocyclic ring; n = 1 or 2; G = (un)substituted C3-6 alkanediyl or alkenediyl (substituents = OH, halo, oxo, aminoalkyl, etc.); X, Y, Z = N, (un)substituted CH; Ar = (un)substituted mono- or bicyclic (hetero)aryl; W = SO2, CO, (un)substituted CH2, bond; or WR1 = atoms to form a benzoxazol-2-yl, benzothiazol-2-yl, benzimidazol-2-yl, 1,2-benzisoxazol-3-yl, 1,2-benzisothiazol-3-yl, or 1,1-dioxo-1,2-benzothiazol-3-yl ring; including stereoisomers and pharmaceutically acceptable salts, esters, and

amides]. Claimed usages include treatment of lupus, rheumatoid arthritis, and particularly asthma, and inhibition of tissue transplant rejection. Approx. 250 individual compds. I were prepared and/or claimed, with detailed prepns. given for 24 compds. For instance, 4-(2-chloro-6-methanesulfonylaminophenyl)piperazine-1-carboxylic acid tert-Bu ester (prepared in 4 steps) was deprotected with TFA and coupled with the corresponding epoxide (prepared in several steps) to give title compound II, a preferred compound. In an assay for inhibition of recombinant human cathepsin S in vitro, II had an IC50 of 0.06 μM. Compound III was another of three specifically preferred compds.

IT 400803-62-5P, 1-[3-(4-Chlorophenyl)-1-(2-hydroxy-3-(3-methyl-4-p-tolylpiperazin-1-yl]propyl]-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of piperazinylpropyl-substituted pyrazolopyridines and analogs as cathepsin S inhibitors)

RN 400803-62-5 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-3-(4-chlorophenyl)-4,5,6,7-tetrahydro-α-[[3-methyl-4-(4-methylphenyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 10 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:71877 CAPLUS
DOCUMENT NUMBER: 136:134783
TITLE: Preparation of piperazine(or piperidine)-1-carboxamides as CCR5 modulators
INVENTOR(S): Bondinell, William E.; Neeb, Michael J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

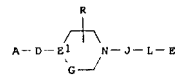
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005819	A1	20020124	WO 2001-US22529	20010713 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

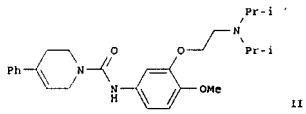
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001080599	A5	20020130	AU 2001-80599	20010713 <--
EP 1313477	A1	20030528	EP 2001-958995	20010713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004038982	A1	20040226	US 2003-343880	20030205
PRIORITY APPLN. INFO.:			US 2000-218509P	P 20000715
			WO 2001-US22529	W 20010713

OTHER SOURCE(S): MARPAT 136:134783
GI



I



II

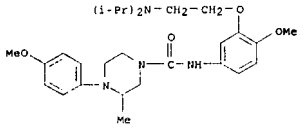
AB The title compds. (I; the basic N atom in moiety E may be optionally quaternized with alkyl or optionally present as the N-oxide; A = (un)substituted (hetero)aryl or (hetero)aryl fused to a saturated or partly unsatd. 5-7 membered ring; D = a bond, CO, SO2, etc.; E1G = NC(R26)2, NC(R26)2C(R26)2, CR27C(R26)2, C:CR26; R26 = H, alkyl; R27 = H, CN, NO2, etc.; R = H, alkyl, O; J = CO, SO2; L = NR30, O, C(R30)2; R30 = H, alkyl; E = 3-(2-diisopropylamino)ethoxy-4-methoxyphenyl, etc.] which are modulators, agonists or antagonists, of the CCR5 receptor, and therefore are useful in the treatment and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis, or idiopathic pulmonary fibrosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, treating and/or preventing rejection of transplanted organs, and inflammatory bowel disease, were prepared. Thus, treating 4-phenyl-1,2,3,6-tetrahydropyridine.HCl with triphosgene in the presence of Et3N in CH2Cl2 followed by addition of 3-(2-diisopropylamino)ethoxy-4-methoxyaniline afforded II. The compds. I showed CCR5 receptor modulator activity having IC50 values in the range of 0.0001-100 μM. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could

provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

IT 391881-79-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine(or piperidine)-1-carboxamides as CCR5 modulators)

RN 391881-79-1 CAPLUS

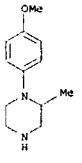
CN 1-Piperazinecarboxamide, N-[3-[2-[bis(1-methylethyl)amino]ethoxy]-4-methoxyphenyl]-4-(4-methoxyphenyl)-3-methyl- (9CI) (CA INDEX NAME)



IT 35947-12-7, 1-(4-Methoxyphenyl)-3-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazine(or piperidine)-1-carboxamides as CCR5 modulators)

RN 35947-12-7 CAPLUS

CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



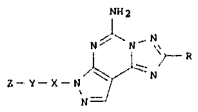
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:886128 CAPLUS
DOCUMENT NUMBER: 136:20084
TITLE: Preparation of 5-amino-pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as adenosine A2a receptor antagonists
INVENTOR(S): Neustadt, Bernard R.; Lindo, Neil A.; Greenlee, William J.; Tulshian, Deen; Silverman, Lisa S.; Xia, Yan; Boyle, Craig D.; Chackalamannil, Samuel
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092264	A1	20011206	WO 2001-US16954	20010524 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2410237	A1	20011206	CA 2001-2410237	20010524 <--
US 2002099061	A1	20020725	US 2001-865071	20010524 <--
US 6630475	B2	20031007		
EP 1283839	A1	20030219	EP 2001-945991	20010524
EP 1283839	B1	20050420		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1451007	A	20031022	CN 2001-813449	20010524
JP 2003535094	T	20031125	JP 2002-500877	20010524
BR 2001011015	A	20050111	BR 2001-11015	20010524
AT 293627	T	20050515	AT 2001-945991	20010524
ES 2237576	T3	20050801	ES 2001-1945991	20010524
NZ 522326	A	20060331	NZ 2001-522326	20010524
CN 1800186	A	20060712	CN 2006-10004929	20010524
HU 200600239	A2	20060728	HU 2006-239	20010524
ZA 2002008898	A	20040301	ZA 2002-8898	20021101
NO 2002005651	A	20030123	NO 2002-5651	20021125
MX 2002PA11625	A	20030327	MX 2002-PA11625	20021125
IN 2002CN01932	A	20050211	IN 2002-CN1932	20021125
HK 1049007	A1	20050916	HK 2003-101315	20030221
US 2004023997	A1	20040205	US 2003-448854	20030530
US 6897216	B2	20050524		
US 2005026932	A1	20050203	US 2004-912834	20040806
US 7067655	B2	20060627		
JP 2006219497	A	20060824	JP 2006-128415	20060502
JP 2007145875	A	20070614	JP 2007-69618	20070316
PRIORITY APPLN. INFO.:			US 2000-207143P	P 20000526
			CN 2001-813449	A3 20010524
			JP 2002-500877	A3 20010524
			US 2001-865071	A3 20010524
			WO 2001-US16954	W 20010524
			US 2003-448854	A3 20030530

OTHER SOURCE(S): MARPAT 136:20084
GI



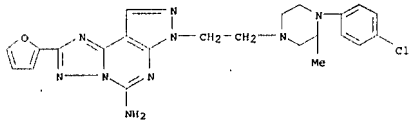
I

AB The title compds. [I; R = (un)substituted Ph, cycloalkenyl, heteroaryl; X = alkylene, COCH2; Y = O, S, CH2S, (CH2)2NH, etc.; Z = (un)substituted Ph, phenylalkyl heteroaryl, etc.; or Z and Y together are substituted piperidinyl or phenyl], useful in the treatment of Parkinson's disease, alone or in combination with other agents for treating Parkinson's disease, were prepared and formulated. E.g., a multi-step synthesis of I [R = 2-furanyl; X = (CH2)2; ZY = 4-(2,4-difluorophenyl)piperazin-1-yl] was described. Compds. I showed Ki of 0.3-57 nM against A2a receptor binding.

IT 377727-38-3P 377727-60-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 5-amino-pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as adenosine A2a receptor antagonists)

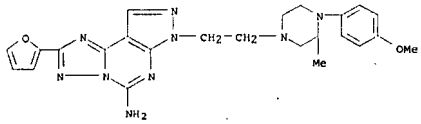
RN 377727-38-3 CAPLUS

CN 7H-Pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-amine, 7-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-2-(2-furanyl)- (9CI) (CA INDEX NAME)



RN 377727-60-1 CAPLUS

CN 7H-Pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-amine, 2-(2-furanyl)-7-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

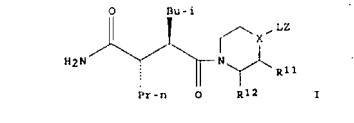


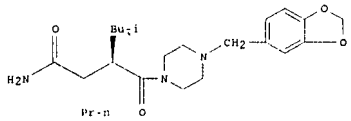
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:747771 CAPLUS
DOCUMENT NUMBER: 135:303912
TITLE: Preparation of succinoylamino-heterocycles as Aβ peptide production inhibitors
INVENTOR(S): Thompson, Lorin Andrew; Kasireddy, Padmaja
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074796	A1	20011011	WO 2001-US10297	20010330 <--
W: AT, AU, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HU, IL, IN, JP, KR, LT, LU, LV, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2404314	A1	20011011	CA 2001-2404314	20010330 <--
EP 1268454	A1	20030102	EP 2001-924498	20010330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
JP 2003529594	T	20031007	JP 2001-572489	20010330
PRIORITY APPLN. INFO.:			US 2000-193490P	P 20000331
			WO 2001-US10297	W 20010330

OTHER SOURCE(S): MARPAT 135:303912
GI





II

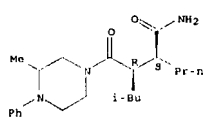
AB Title compds. [I; R11 = H, CH3, LZ, OH, CH2OH, CONH2, COOCH2CH3; R12 = H, LZ; LZ = CH3, CH2C6H5, 2-CH3C6H4, 3-CF3C6H4, 4-FC6H4, CH2CH2OH, CH2CH3, CH2CH:CH2C6H5, 2,6-(CH3)2C6H3, R10; R10 = CH2COOCH2CH3, COCH3, (4-ClC6H4)2CH; X = CH, N, CCOOCH2CH3, CN(CH3)2, COH, CCH3, CCOCH3, CCONH2, CCOCH2CH3, etc.] are prepared and are useful as remedies of neurol. disorders related to β-amyloid production such as Alzheimer's disease and Down's syndrome. Title compds. I inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent formation of neurol. deposits of amyloid protein. Thus, the title compound II was prepared and in vitro tested for Aβ peptide accumulation inhibition.

IT 365538-73-4P 365539-26-0P 365539-46-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of succinoylaminoheterocycles as Aβ peptide production inhibitors)

RN 365538-73-4 CAPLUS

CN 1-Piperazinebutanamide, 3-methyl-β-(2-methylpropyl)-γ-oxo-4-phenyl-α-propyl-, (αS,βR)- (9CI) (CA INDEX NAME)

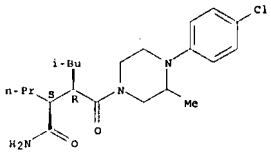
Absolute stereochemistry.



RN 365539-26-0 CAPLUS

CN 1-Piperazinebutanamide, 4-(4-chlorophenyl)-3-methyl-β-(2-methylpropyl)-γ-oxo-α-propyl-, (αS,βR)- (9CI) (CA INDEX NAME)

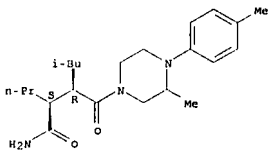
Absolute stereochemistry.



RN 365539-46-4 CAPLUS

CN 1-Piperazinebutanamide, 3-methyl-4-(4-methylphenyl)-β-(2-methylpropyl)-γ-oxo-α-propyl-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

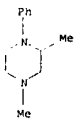
L9 ANSWER 13 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:731861 CAPLUS
DOCUMENT NUMBER: 136:14987
TITLE: Structure-Affinity Relationships of a Unique Nicotinic Ligand: N1-Dimethyl-N4-phenylpiperazinium Iodide (DMPP)
AUTHOR(S): Romanelli, Maria Novella; Manetti, Dina; Scapecchi, Serena; Borea, Pier Andrea; Dei, Silvia; Bartolini, Alessandro; Ghelardini, Carla; Gualtieri, Fulvio; Guandalini, Luca; Varani, Katia
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy
SOURCE: Journal of Medicinal Chemistry (2001), 44(23), 3946-3955
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English

AB DMPP is a well-known nicotinic agonist that does not fit any proposed pharmacophore for nicotinic binding and represents a unique ligand among the hundreds of nicotinic agonists studied in the past decades. A systematic modulation of the chemical structure of DMPP, aimed to establish its structure-affinity relationships, is reported. The research has allowed to identify mols. with affinities for $\alpha 4\beta 2$ receptors in the low nanomolar range, some 2 orders of magnitude lower than the lead compound The agonistic properties of the most interesting compds. have been assessed by measuring their analgesic activity on mice (hot-plate test). Another result of the research was the identification of DMPP analogs with Ki = 90 nM and 180 nM, that maintain affinity for the central nicotinic receptor when the ammonium function is changed into an aminic one and are therefore possible leads for drug development in neurodegenerative diseases.

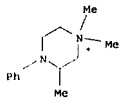
IT 33905-49-6P 378758-81-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure-activity relationships of a nicotinic ligand, DMPP)

RN 33905-49-6 CAPLUS
CN Piperazine, 2,4-dimethyl-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 378758-81-7 CAPLUS
CN Piperazinium, 1,1,3-trimethyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



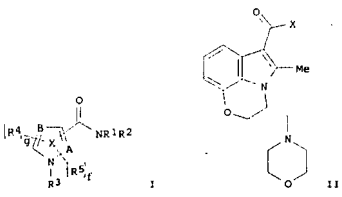
● I⁻

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:597958 CAPLUS
DOCUMENT NUMBER: 135:166827
TITLE: Preparation of 1H-indole-3-carboxamides, 1H-indazole-3-carboxamides, 1H-pyrido[4,3-b]indol-1-ones and pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamides as cannabinoid receptor modulators for treating respiratory and non-respiratory diseases
INVENTOR(S): Leftheris, Katerina; Zhao, Rulin; Chen, Bang-Chi; Kiener, Peter; Wu, Hong; Pandit, Chennagiri R.; Wrobleski, Stephen; Chen, Ping; Hynes, John, Jr.; Longphre, Malinda; Norris, Derek J.; Spergel, Steven; Tokarski, John
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; et al.
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058869	A2	20010816	WO 2001-US4131	20010208 <--
WO 2001058869	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2399791	A1	20010816	CA 2001-2399791	20010208 <--
AU 200134958	A	20010820	AU 2001-34958	20010208 <--
EP 1254115	A2	20021106	EP 2001-907144	20010208 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502642	T	20040129	JP 2001-558420	20010208
PRIORITY APPLN. INFO.:			US 2000-181818P	P 20000211
			WO 2001-US4131	W 20010208
OTHER SOURCE(S):	MARPAT 135:166827			

GI

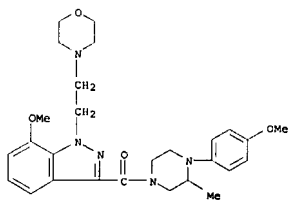


I II

AB The title compds. [I; A, B = C, N so that ring X = pyrrole, pyrazole or imidazole (wherein when A = N, the group CONR1R2 is attached to atom C-3 and R5 does not exist; and when A = C, one of CONR1R2 and R5 is attached to A and the other to atom C-3; and when B = C, two R4 groups attached to B and atom C-5, resp., form a fused 6-membered heteroaryl); f = 0-1; g = 1-2; R1, R2 = H, alkyl, heterocycloalkyl, etc.; R2 together with R1 or R5 forms a 5-6 membered heterocyclo; R3 = H, alkyl, aryl, etc.; R4 is attached to atom C-5 and optionally B and is H, alkyl, aryl, etc.; R5 is attached to A or atom C-3 and is H, alkyl, aryl, etc.; R5 together with R2 forms a heterocyclo], useful as cannabinoid receptor modulators (no data given) for treating respiratory and non-respiratory leukocyte-activation associated diseases, were prepared Thus, reacting the acid chloride II [X = Cl] (multi-step synthesis given) with 2,2,6,6-tetramethylcyclohexylamine afforded the pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamide II [X = 2,2,6,6-tetramethylcyclohexylamino].

IT 354572-38-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1H-indole-3-carboxamides, 1H-indazole-3-carboxamides, 1H-pyrido[4,3-b]indol-1-ones and pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamides as cannabinoid receptor modulators for treating respiratory and non-respiratory diseases)

RN 354572-38-6 CAPLUS
CN Piperazine, 4-[[7-methoxy-1-[2-(4-morpholinyl)ethyl]-1H-indazol-3-yl]carbonyl]-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

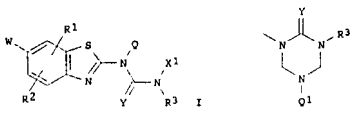


L9 ANSWER 15 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:581863 CAPLUS
DOCUMENT NUMBER: 135:152801
TITLE: Preparation of 2-benzothiazolyl ureas as protein kinase inhibitors
INVENTOR(S): Cusack, Kevin P.; Scott, Barbara; Arnold, Lee D.; Ericsson, Anna
PATENT ASSIGNEE(S): Basf Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001057008	A1	20010809	WO 2001-US3803	20010206 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2398754	A1	20010809	CA 2001-2398754	20010206 <--
EP 1254123	A1	20021106	EP 2001-908878	20010206 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001008085	A	20030318	BR 2001-8085	20010206
HU 200300359	A2	20030628	HU 2003-359	20010206
JP 2003521543	T	20030715	JP 2001-556958	20010206
US 2003153568	A1	20030814	US 2001-777554	20010206
US 7091227	B2	20060815		
ZA 2002006235	A	20040213	ZA 2002-6235	20020805
IN 2002MN01057	A	20040529	IN 2002-MN1057	20020805
NO 2002003713	A	20021004	NO 2002-3713	20020806 <--
MX 2002PA07632	A	20040823	MX 2002-PA7632	20020807
BG 107062	A	20030430	BG 2002-107062	20020904

PRIORITY APPLN. INFO.: US 2000-180841P P 20000207
WO 2001-US3803 W 20010206

OTHER SOURCE(S): MARPAT 135:152801
GI

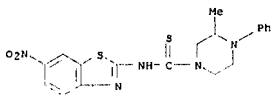


I II

AB The title compds. [I; Q = H or a bond which is taken together with X1 and two N atoms to which Q and X1 are attached and C:Y group to which the two N atoms are attached to form II; Q1 = alkyl; Y = O, S; W = H, Cl, Br, etc.; X1 = H, alkyl, hydroxyalkyl or a bond which is taken together with R3 to form pyrrolidino, piperazino or morpholino; R1, R2 = H, halo, OH, etc.; R3 = H, alkyl, aryl, etc.], useful as inhibitors of serine/threonine and tyrosine kinases such as FGFR, PDGFR, KDR, VEGFR-3, Tie-2, Tie-1; Lck, Fyn, Blk, Lyn, Src, cdc2 (cdk1) or Plk-1 (biol. data given), were prepared and formulated. Thus, reacting 3,5-dimethoxyphenyl isocyanate with 2-amino-6-nitrobenzothiazole in the presence of Et3N in PhMe afforded I [W = NO2; Q, X1, R1, R2 = H; Y = O; R3 = 3,5-(MeO)2C6H3]. In particular, compds. I are useful as inhibitors of tyrosine kinases that are important in hyperproliferative diseases, especially in cancer and in the process of angiogenesis.

IT 352527-26-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-benzothiazolyl ureas as protein kinase inhibitors)

RN 352527-26-5 CAPLUS
CN 1-Piperazinecarbothioamide, 3-methyl-N-(6-nitro-2-benzothiazolyl)-4-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

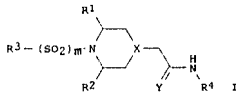
L9 ANSWER 16 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:472725 CAPLUS
DOCUMENT NUMBER: 135:76897
TITLE: Synthesis and use of substituted piperidine and piperazine derivatives (e.g. N-(sulfonyl)aryl, N-alkylcarboxamido piperazines) as antagonists of the

P2X7 receptor
INVENTOR(S): Meghani, Premji; Bennion, Colin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046200	A1	20010628	WO 2000-SE2580	20001218 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2394095	A1	20010628	CA 2000-2394095	20001218 <--
BR 2000016543	A	20020917	BR 2000-16543	20001218 <--
EP 1242427	A1	20020925	EP 2000-989102	20001218 <--
EP 1242427	B1	20030813		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518126	T	20030603	JP 2001-547110	20001218
AT 247123	T	20030815	AT 2000-989102	20001218
NZ 519498	A	20040227	NZ 2000-519498	20001218
AU 776592	B2	20040916	AU 2001-25648	20001218
ZA 2002004307	A	20030829	ZA 2002-4307	20020529
US 2003013721	A1	20030116	US 2002-168094	20020617
US 6969713	B2	20051129		
NO 2002003037	A	20020822	NO 2002-3037	20020621 <--
MX 2002PA06261	A	20021205	MX 2002-PA6261	20020621 <--
US 2005272745	A1	20051208	US 2005-125335	20050510

PRIORITY APPLN. INFO.: SE 1999-4738 A 19991222
WO 2000-SE2580 W 20001218
US 2002-168094 A1 20020617

OTHER SOURCE(S): MARPAT 135:76897
GI



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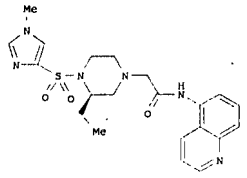
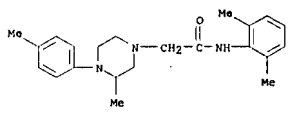


II

AB Compds. of formula I, their preparation and use as P2X7 receptor antagonists are claimed [wherein: X = N or CR5; Y = O, S, or NR6; R1, R2 = H or alkyl but do not simultaneously represent H, or R1R2 = CH2ZCH2; Z = bond, O, S, CH2, or NR7; m = 0 or 1; R3 = 5-10 membered unsatd. (substituted) ring which may contain 1-4 heteroatoms chosen from N, O or S; R4 = ortho-substituted Ph/pyridinyl, said rings may be further substituted, or R4 = 9-10 membered unsatd. (substituted) bicyclic ring system which may contain 1-4 heteroatoms chosen from N, O or S; R5 = H, OH or alkoxy; R6 = H, CN, NO2, OH, alkyl or alkoxy; R7 = H, alkyl; with addnl. provisos]. More than 100 synthetic examples are provided. For instance, (R)-3-ethyl-1-phenylmethylpiperazine (prepared in 3 steps from (R)-N-Boc-2-aminobutyric acid) was reacted with 1-methylimidazole-4-sulfonyl chloride in the presence of base to give the corresponding N-benzyl piperazine sulfonamide. This intermediate was debenzylated and reacted with 2-chloro-N-(quinolin-5-yl)acetamide to yield II. The invention compds. were tested for antagonist activity at the P2X7 receptor using benzoylbenzoyl ATP (bbATP, a P2X7 agonist) as a control for P2X7 receptor activation. Compds. of the invention had pIC50 (neg. log of the concentration of test compound necessary to reduce the bbATP agonist activity by 50%) > 5.0. Compds. I are used for treatment of rheumatoid arthritis and COPD, and for effecting immunosuppression.

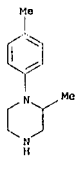
IT 347194-32-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; synthesis and use of substituted piperidine and piperazine derivs. (e.g. N-(sulfonyl)aryl, N-alkylcarboxamido piperazines) as antagonists of the P2X7 receptor)

RN 347194-32-5 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)-3-methyl-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)



IT 35947-11-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; synthesis and use of substituted piperidine and piperazine derivs. (e.g. N-(sulfonyl)aryl, N-alkylcarboxamido piperazines) as antagonists of the P2X7 receptor)

RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 . ANSWER 17 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:338558 CAPLUS
DOCUMENT NUMBER: 134:340709
TITLE: Preparation of substituted dipeptides having NOS inhibiting activity
INVENTOR(S): Shima, Ichiro; Ohkawa, Takehiko; Ohne, Kazuhiko; Sato, Kentaro; Ishibashi, Naoki; Imamura, Kenichiro
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032690	A1	20010510	WO 2000-JP7579	20001027 <--
W: BR, CA, CN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1226159	A1	20020731	EP 2000-970164	20001027 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY

JP 2003513104	T	20030408	JP 2001-535389		20001027
US 6825200	B1	20041130	US 2002-111412		20020506
PRIORITY APPLN. INFO.:			AU 1999-3868	A	19991104
			WO 2000-JP7579	W	20001027

OTHER SOURCE(S): MARPAT 134:340709

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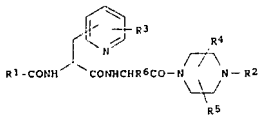


I

AB Dipeptides I [R1 is benzofuranyl or styryl substituted by halogen; R2 is (un)substituted Ph, pyridyl, thienyl, or thiazolyl; R3, R6 = H or lower alkoxy; R4, R5 = H, lower alkyl or optionally protected hydroxy(lower)alkyl] or their pharmaceutically acceptable salts were prepared for use in the prevention and/or treatment of nitric oxide-mediated diseases. Thus, 5-chloro-N-[(1S)-2-[[2-[4-(4-chlorophenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxo-1-(2-pyridylmethyl)ethyl]-1-benzofuran-2-carboxamide (II) was prepared via amidation reaction and showed 100% inhibition of nitric acid. The combination of compound II and FK507 dramatically prolonged graft survival in rat cardiac allograft.

IT 337530-63-9P

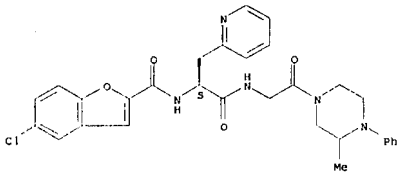
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted dipeptides having NOS inhibiting activity)

RN 337530-63-9 CAPLUS

CN 2-Pyridinepropanamide, α-[[(5-chloro-2-benzofuranyl)carbonyl]amino]-N-[2-(3-methyl-4-phenyl-1-piperazinyl)-2-oxoethyl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



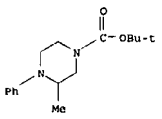
IT 337530-61-7P 337530-62-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted dipeptides having NOS inhibiting activity)

RN 337530-61-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 3-methyl-4-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 337530-62-8 CAPLUS

CN Piperazine, 2-methyl-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

●x HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:228874 CAPLUS

DOCUMENT NUMBER: 134:266313

TITLE: Preparation and use of substituted piperazine derivatives as MTP inhibitors

INVENTOR(S): Lehmann-Lintz, Thorsten; Heckel, Armin; Thomas, Leo; Mark, Michael

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021604	A1	20010329	WO 2000-EP9146	20000919 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19945594	A1	20010329	DE 1999-19945594	19990923 <--
CA 2388759	A1	20010329	CA 2000-2388759	20000919 <--
EP 1228053	A1	20020807	EP 2000-969264	20000919 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003509505	T	20030311	JP 2001-524983	20000919
JP 3908034	B2	20070425		
MX 2002PA02838	A	20030721	MX 2002-PA2838	20020314
US 6818644	B1	20041116	US 2002-89024	20020701
PRIORITY APPLN. INFO.:			DE 1999-19945594	A 19990923
			WO 2000-EP9146	W 20000919

OTHER SOURCE(S): MARPAT 134:266313

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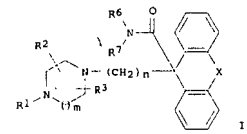

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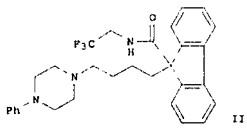


II

AB Compds. of formula I [wherein; n is 1-5; m is 1 or 2; X is a bond, O, CH2(CH2), imino or N-alkyl-imino; R1 is (substituted) aryl or heteroaryl; R2, R3 are hydrogen or alkyl; R6, R7 are H, (fluoro)alkyl, cycloalkyl, Ph, heteroaryl, etc., or NR6R7 may form a 3-7 membered ring.]. Thirty eight examples of I are prepared (e.g. II). Compound II was prepared by alkylation of 9-fluorenecarboxylic acid with 1,4-dibromobutane. The alkylated intermediate was converted to its acyl chloride derivative, and treated with 2,2,2-trifluoroethylamine to provide pivotal intermediate, 9-(4-bromobutyl)-9H-fluorene-9-(2,2,2-trifluoroethylcarboxamide). Alkylation of 1-phenylpiperazine with this intermediate yields II. Three solid oral dosage formulations of compds. I are disclosed. Compds. of

formula I are said to be inhibitors of the microsomal triglyceride-transfer protein (MTP). Use of compds. I to prepare drugs which lower plasma levels of atherogenic lipoproteins is claimed.

IT 331767-25-0P

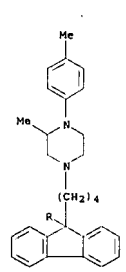
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and use of substituted piperazine derivs.)

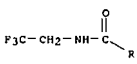
RN 331767-25-0 CAPLUS

CN 9H-Fluorene-9-carboxamide, 9-[4-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]butyl]-N-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:208282 CAPLUS

DOCUMENT NUMBER: 134:237472

TITLE: Preparation of 1-amino-3-thienoisoxazolylphenoxy-2-propanols as dopamine D4 antagonists

INVENTOR(S): Fink, David M.; Freed, Brian S.; Hrib, Nicholas J.; Kosley, Raymond W., Jr.; Lee, George E.; Merriman, Gregory N.; Rauckman, Barbara S.

PATENT ASSIGNEE(S): Aventis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 157 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019833	A1	20010322	WO 2000-US24962	20000913 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2383340	A1	20010322	CA 2000-2383340	20000913 <--
BR 2000014515	A	20020625	BR 2000-14515	20000913 <--
EP 1216250	A1	20020626	EP 2000-964969	20000913 <--
EP 1216250	B1	20031119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
HU 200203526	A2	20030128	HU 2002-3526	20000913
EE 200200135	A	20030415	EE 2002-135	20000913
AT 254621	T	20031215	AT 2000-964969	20000913
PT 1216250	T	20040430	PT 2000-964969	20000913
ES 2209995	T3	20040701	ES 2000-964969	20000913
TW 530060	B	20030501	TW 2000-89118850	20000914
NO 2002001251	A	20020510	NO 2002-1251	20020313 <--
MX 2002PA02695	A	20020730	MX 2002-PA2695	20020313 <--
ZA 2002001762	A	20030602	ZA 2002-1762	20020321
US 7125903	B1	20061024	US 2002-88250	20021223
US 2007004695	A1	20070104	US 2006-459068	20060721
PRIORITY APPLN. INFO.:			US 1999-396081	A1 19990914
			US 1999-229355P	P 19990914
			WO 2000-US24962	W 20000913
			US 2002-88250	A3 20021223

OTHER SOURCE(S): MARPAT 134:237472

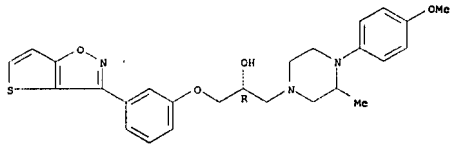
AB RZOCH2CR1R2CH2NR3R4 [I; R = e.g., thieno[2,3-d]isoxazol-3-yl; R1 = OH or alkoxy; R2,R4 = H or alkyl; R3 = CH2R5, CH2CH(OH)R5, indanyl, etc.; R5 = cyclohex(en)yl, (hetero)aryl, etc.; Z = phenylene] were prepared Thus, 3-bromothiophene was acylated by 3-(MeO)C6H4COCl and the oximated product cyclized to give, after O-demethylation, 3-RC6H4OH [R = thieno[2,3-d]isoxazol-3-yl] which was etherified by (R)-glycidyl tosylate and the product aminated by PhCHMeNH2 to give (R)-3-RC6H4OCH2CH(OH)CH2NMeCH2Ph (R as above). Data for biol. activity of I were given.

IT 330651-02-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-amino-3-thienoisoxazolylphenoxy-2-propanols as dopamine D4 antagonists)

RN 330651-02-0 CAPLUS

CN 1-Piperazineethanol, 4-(4-methoxyphenyl)-3-methyl- α-[(3-thieno[2,3-d]isoxazol-3-ylphenoxy)methyl]-, (αR)- (9CI) (CA INDEX NAME)

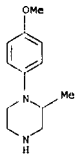
Absolute stereochemistry.



IT 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1-amino-3-thienoisoxazolylphenoxy-2-propanols as dopamine D4 antagonists)

RN 35947-12-7 CAPLUS

CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:115118 CAPLUS
DOCUMENT NUMBER: 134:163065
TITLE: Preparation of hydroxamic acid and N-formyl hydroxylamine derivatives as antibacterial agents
INVENTOR(S): Pratt, Lisa Marie; Keavey, Kenneth Noel; Pain, Gilles Denis; Mounier, Laurent Franck
PATENT ASSIGNEE(S): British Biotech Pharmaceuticals Limited, UK
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001010834	A2	20010215	WO 2000-GB3078	20000810 <--
WO 2001010834	A3	20010628		
W: AE, AU, BR, BY, CA, CN, CZ, DZ, EE, GB, GE, HU, ID, IL, IN, IS, JP, KE, KR, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, US, VN, ZA, ZW				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CN 1373754	A	20000810	CN 2000-812860	20000810 <--
CA 2379061	A1	20010215	CA 2000-2379061	20000810 <--
EP 1202968	A2	20020508	EP 2000-949820	20000810 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY				
BR 2000013112	A	20020611	BR 2000-13112	20000810 <--
TR 200200360	T2	20020621	TR 2002-360	20000810 <--
HU 200202514	A2	20021128	HU 2002-2514	20000810 <--
JP 2003506438	T	20030218	JP 2001-515301	20000810
AU 766881	B2	20031023	AU 2000-63080	20000810
NZ 517239	A	20040924	NZ 2000-517239	20000810
CN 1704402	A	20051207	CN 2005-10081198	20000810
RU 2269525	C2	20060210	RU 2002-106409	20000810
CN 101007784	A	20070801	CN 2007-10007364	20000810
ZA 2002001093	A	20030507	ZA 2002-1093	20020207
NO 2002000621	A	20020409	NO 2002-621	20020208 <--
MX 2002PA01394	A	20020812	MX 2002-PA1394	20020208 <--
US 6846825	B1	20050125	US 2002-49131	20020710
US 2005065095	A1	20050324	US 2004-953788	20040930
US 7186719	B2	20070306		
PRIORITY APPLN. INFO.:			GB 1999-18869	A 19990810
			GB 1999-27093	A 19991116
			CN 2000-812860	A3 20000810
			WO 2000-GB3078	W 20000810
			US 2002-49131	A3 20020710

OTHER SOURCE(S): MARPAT 134:163065

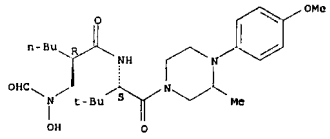
AB Selected compds. QCH(R1)CH(R2)C(O)A (I) and pharmaceutical and veterinary compns. comprising such compds. are antibacterial agents with respect to a range of Gram-pos. and Gram-neg. organisms. In I, Q = -N(OH)C(O)H or -C(O)NH(OH); R1 = H, C1-C6 alkyl or C1-C6 alkyl substituted by ≥ halogen atoms, or, except when Q is -N(OH)C(O)H, hydroxy, C1-C6 alkoxy, C1-C6 alkenyloxy, amino, C1-C6 alkylamino, or di-(C1-C6 alkyl)amino; R2 = substituted or unsubstituted C1-C6 alkyl, cycloalkyl(C1-C6 alkyl)- or aryl(C1-C6 alkyl)-; and A = -NHCHR4C(O)NR5R6 or -NR5R6, wherein R4 = side chain of a natural or non-natural α-amino acid, and R5 and R6 when taken together with the N atom to which they are attached form a saturated heterocyclic 1st ring of 5 to 7 atoms (piperidine and piperazine in the examples). In general, the compds. of the examples are more active against the Gram pos. S. capitis than the Gram neg. E. coli. Test results are also reported for 2R-cyclopentylmethyl-3-(formylhydroxyamino)-N-(1S-[4-[4-(4-hydroxypiperidine-1-carbonyl)phenoxy]piperidine-1-carbonyl]-2,2-dimethylpropyl)propionamide against certain respiratory tract pathogens. Although the methods of preparation are not claimed, .apprx.95 example prepns. are included.

IT 325795-50-4P, 2R-[(Formylhydroxyamino)methyl]hexanoic acid (1S-[4-(4-methoxyphenyl)-3-methylpiperazine-1-carbonyl]-2,2-dimethylpropyl)amide 325795-56-0P, N-Hydroxy-N-{2R-[4-(4-methoxyphenyl)-3-methylpiperazine-1-carbonyl]hexyl}formamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydroxamic acid and N-formyl hydroxylamine derivs. as antibacterial agents)

RN 325795-50-4 CAPLUS

CN Hexanamide, 2-[(formylhydroxyamino)methyl]-N-[(1S)-1-[[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]carbonyl]-2,2-dimethylpropyl]-, (2R)- (9CI) (CA INDEX NAME)

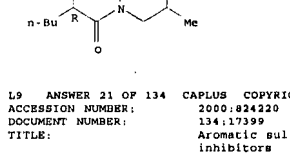
Absolute stereochemistry.



RN 325795-56-0 CAPLUS

CN Piperazine, 4-[(2R)-2-[[(formylhydroxyamino)methyl]-1-oxohexyl]-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



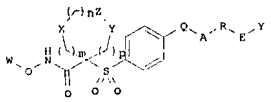
L9 ANSWER 21 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:824220 CAPLUS
DOCUMENT NUMBER: 134:17399
TITLE: Aromatic sulfone hydroxamic acid metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.; Carroll, Jeffrey N.; Decrescenzo, Gary A.; Fobian, Yvette M.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Hockerman, Susan L.; Howard, Susan C.; Kolodziej, Stephen A.; Li, Madeleine Hui; Mischke, Deborah A.; Rico, Joseph G.; Stehle, Nathan W.; Tollefson, Michael B.; Vernier, William F.; Villamil, Clara I.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 616 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069821	A1	20001123	WO 2000-US6719	20000515 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,				

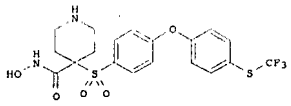
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6750228	B1	20040615	US 2000-570731		20000512
CA 2372934	A1	20001123	CA 2000-2372934		20000515 <--
EP 1183239	A1	20020306	EP 2000-930088		20000515 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 2000010562	A	20030610	BR 2000-10562		20000515
JP 2003520196	T	20030702	JP 2000-618238		20000515
AU 766792	B2	20031023	AU 2000-47970		20000515
NZ 515217	A	20040430	NZ 2000-515217		20000515
ZA 2001009006	A	20021202	ZA 2001-9006		20011031 <--
NO 2001005543	A	20020110	NO 2001-5543		20011113 <--
MX 2001PA11569	A	20050620	MX 2001-PA11569		20011113
PRIORITY APPLN. INFO.:			US 1999-311837	A	19990514
			US 2000-570731	A	20000512
			US 1997-66007P	P	19971114
			US 1998-95347P	P	19980804
			US 1998-101080P	P	19980918
			US 1999-256948	B2	19990224
			WO 2000-US6719	W	20000515

OTHER SOURCE(S): MARPAT 134:17399
GI



I

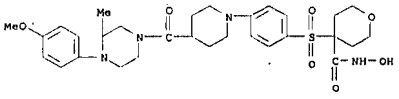


II

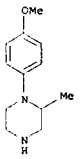
AB A treatment process is disclosed that comprises administering an effective amount of an aromatic sulfone hydroxamic acid I [W = H, cation, certain acyl or thioacyl groups; m, n, p = 0-2; (m+n+p) = 1 to 4; one of X, Y, and Z = CO, NH or derivs., O, S, SO, SO2, etc., and the other two = (un)substituted CH2; or XZ or ZY = (un)substituted NHCO, NHSO, NHSO2, SS, OCO, etc., and the other one = (un)substituted CH2; or n = 0 and XZY = atoms to complete various N/O/S heterocycles; Q = 5- to 7-membered heterocycle with 1-2 N atoms, one bound to Ph, and with -AREY bound in para-type positions; A =

bond, O, S, (un)substituted NH, COO, OCO, CH:CH, C.tplbond.C, N:N, NHNH, NHCOO, (un)substituted CONH, NHCO, etc.; R = alkylene, arylene, heteroarylene, etc., with provisos; E = bond, CONH, NHCO, CO, SO2, NHSO2, SO2NH, S, etc.; Y = absent, H, alkyl, alkoxy, aryl, aryloxy, heteroaryl, etc.) to a host having a condition associated with pathol. matrix metalloprotease (MMP) activity. I exhibit excellent inhibitory activity of one or more MMP enzymes, such as MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibition of (at least) MMP-1. Also disclosed are metalloprotease inhibitor compds. having such selective activities, processes for manufacture of such compds., and pharmaceutical compns. using such inhibitors. The compds. are potentially useful against a wide variety of conditions, notably as antiinflammatory, antiangiogenesis, and antitumor agents. Over 900 example compds. are listed, most with supporting phys. data, and many with synthetic details. For instance, Et N-(tert-butoxycarbonyl)-4-(4-fluorophenylsulfonyl)-4-piperidinecarboxylate (preparation given) was subjected to a sequence of: (1) etherification with 4-(CF3S)C6H4OH (100%); (2) alkaline hydrolysis of the ester (100%); (3) amidation with THP-ONH2 (45%); and (4) acid deprotection of the THP ether (40%), to give title compound II.HCl. The latter salt selectively inhibited MMP-13 with IC50 0.2 nM, and MMP-2 with IC50 0.1 nM, but with IC50 >10,000 nM against MMP-1.

IT 308821-73-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aromatic sulfone hydroxamic acids as metalloprotease inhibitors)
RN 308821-73-0 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[4-[[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]carbonyl]-1-piperidinyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



IT 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of aromatic sulfone hydroxamic acids as metalloprotease inhibitors)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

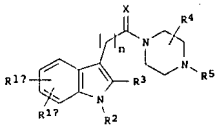


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 22 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:628119 CAPLUS
DOCUMENT NUMBER: 133:222745
TITLE: Preparation of 1-[(2-arylindol-3-yl)-1-oxoalkyl]piperazines as antagonists of tachykinins
INVENTOR(S): Chapman, Kevin T.; Dinnell, Kevin; Elliott, Jason Matthew; Hollingworth, Gregory John; Hutchins, Steven Michael; Shaw, Duncan Edward; Willoughby, Christopher Alan
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051984	A1	20000908	WO 2000-GB650	20000223 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6518273	B1	20030211	US 2001-914893	20010904
PRIORITY APPLN. INFO.:			GB 1999-5010	A 19990304
			WO 2000-GB650	W 20000223

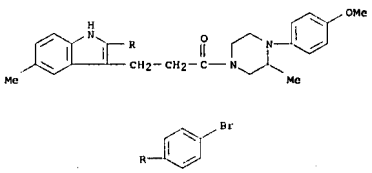
OTHER SOURCE(S): MARPAT 133:222745
GI



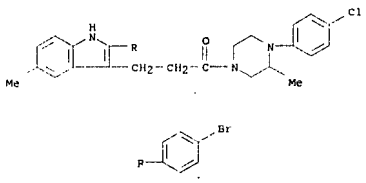
I

AB The title compds. [I; R1a, R1b = H, alkyl, alkoxy, etc.; R2 = H, alkyl, fluoroalkyl, etc.; R3 = (un)substituted Ph, biphenyl, naphthyl; R4 = H, alkyl, O (to form carbonyl), etc.; R5 = alkyl, cycloalkyl, cycloalkylalkyl, etc.; X = O, S; n = 1-4] and their pharmaceutically acceptable salts which are potent receptor antagonists of tachykinins, especially of the neurokinin-1 (substance P) receptor (no data), and useful in the treatment or prevention of depression, anxiety, pain, inflammation, migraine, emesis or postherpetic neuralgia, were prepared E.g., a synthesis of the piperazine I [R1a = 5-Me; R1b = H; R2 = H; R3 = 4-BrC6H4; R4 = H; R5 = 2-MeOC6H4; X = O; n = 2] was given. Compds. I are effective at 0.05-10 mg/kg/day in the treatment of conditions associated with an excess of tachykinins.

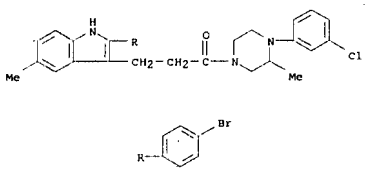
IT 290830-78-3P 290830-83-0P 290831-26-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-[(2-arylindol-3-yl)-1-oxoalkyl]piperazines as antagonists of tachykinins)
RN 290830-78-3 CAPLUS
CN Piperazine, 4-[3-[2-(4-bromophenyl)-5-methyl-1H-indol-3-yl]-1-oxopropyl]-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 290830-83-0 CAPLUS
CN Piperazine, 4-[3-[2-(4-bromophenyl)-5-methyl-1H-indol-3-yl]-1-oxopropyl]-1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 290831-26-4 CAPLUS
CN Piperazine, 4-[3-[2-(4-bromophenyl)-5-methyl-1H-indol-3-yl]-1-oxopropyl]-1-(3-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

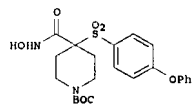
L9 ANSWER 23 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:608722 CAPLUS
DOCUMENT NUMBER: 133:193079
TITLE: Preparation of arylsulfonylheterocyclylhydroxamic acids and related compounds as matrix metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.; Carroll, Jeffery N.; De Crescenzo, Gary A.; Fobian, Yvette M.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Hanson, Gunnar J.; Hockerman, Susan L.; Howard, Susan C.; Kolodziej, Steve A.; Li, Hui; Mischke, Deborah A.; Rico, Joseph G.; Stehle, Nathan W.; Tollefson, Michael B.; Vernier, William F.; Villamil, Clara I.; Rao, Shashidahar N.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 851 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050396	A1	20000831	WO 2000-US2518	20000222 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001039287	A1	20011108	US 1999-256948	19990224 <--
CA 2371876	A1	20000831	CA 2000-2371876	20000222 <--
AU 200034785	A	20000914	AU 2000-34785	20000222 <--
HU 200200239	A2	20020629	HU 2002-239	20000222 <--
EP 1230219	A1	20020814	EP 2000-913317	20000222 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000008491	A	20020917	BR 2000-8491	20000222 <--
JP 2002537378	T	20021105	JP 2000-600979	20000222 <--
NZ 513648	A	20040227	NZ 2000-513648	20000222
NO 2001003963	A	20011023	NO 2001-3963	20010815 <--
ZA 2001006780	A	20020816	ZA 2001-6780	20010816 <--
IN 2001CN01174	A	20050304	IN 2001-CN1174	20010821
MX 2001PA08568	A	20020408	MX 2001-PA8568	20010823 <--
US 2002177588	A1	20021128	US 2001-954451	20010917 <--
US 6750233	B2	20040615		

PRIORITY APPLN. INFO.:

US 1999-256948	A	19990224
US 1997-66007P	P	19971114
US 1998-95347P	P	19980804
US 1998-95501P	P	19980806
US 1998-101080P	P	19980918
WO 2000-US2518	W	20000222

OTHER SOURCE(S): MARPAT 133:193079
GI



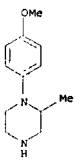
I

AB A process for treating conditions associated with pathol. matrix metalloproteinase (MMP) activity comprises administration of compds. having inhibitory activity against >1 of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibition of MMP-1. The compds. are of the form HONHCOCR1R2SO2R3 [R1, R2 = H; R1R2 = atoms to form a 5-8 membered ring containing 1-3 heteroatoms; R3 = (substituted) aryl, heteroaryl]. Thus, 4-PhOC6H4SH was heated in Me2SO to give the disulfide dimer, which in THF was added to a mixture of Et N-tert-butoxycarbonylisonipecotate (preparation given) and LDA in THF at -60° to room temperature to give 40% sulfide, which was oxidized with m-ClC6H4CO(OOH) to give 59% sulfone. The Et ester was saponified with NaOH in EtOH/H2O to give 100% acid, which in DMF was

treated with hydroxybenzotriazole, EDC, 4-methylmorpholine, and aqueous NH2OH to give title compound I. I inhibited MMP-2 with IC50 = 0.2 nM. Pharmacol., pharmacokinetic, and toxicol. data are given for selected compds.

IT 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of arylsulfonylheterocyclylhydroxamic acids and related compds. as matrix metalloprotease inhibitors)

RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:513446 CAPLUS
DOCUMENT NUMBER: 133:129863
TITLE: Heterocyclic compound modulators of the CCR5 receptor, preparation thereof, and therapeutic use
INVENTOR(S): Bondinell, William E.; Neeb, Michael J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042852	A1	20000727	WO 2000-US1908	20000125 <--
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1146790	A1	20011024	EP 2000-909984	20000125 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002535256	T	20021022	JP 2000-594326	20000125 <--

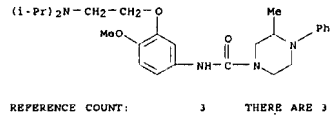
PRIORITY APPLN. INFO.:

US 1999-117044P	P	19990125
WO 2000-US1908	W	20000125

OTHER SOURCE(S): MARPAT 133:129863
AB Substituted heterocyclic compds. are provided which are modulators, agonists or antagonists of the CCR5 receptor. Also disclosed is the treatment and prevention of disease states mediated by CCR5, including, but no limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted heterocyclic compds. which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

IT 286387-94-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclic compound modulators of CCR5 receptor, preparation, and therapeutic use)

RN 286387-94-8 CAPLUS
CN 1-Piperazinecarboxamide, N-[3-[2-[bis(1-methylethyl)amino]ethoxy]-4-methoxyphenyl]-3-methyl-4-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

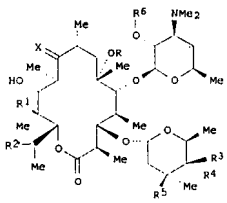
L9 ANSWER 25 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:388555 CAPLUS
DOCUMENT NUMBER: 133:17747
TITLE: Preparation of 6-O-substituted erythromycins as antibacterial agents
INVENTOR(S): Or, Yat Sun; Clark, Richard F.; Ma, Zhenkun; Griesgraber, George; Li, Leping; Chu, Daniel T.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 128 pp., Cont.-in-part of U.S. Ser. No. 646,477, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6075011	A	20000613	US 1997-841038	19970429 <--
CA 2253330	A1	19971113	CA 1997-2253330	19970506 <--
CA 2253330	C	20060725		
WO 9742206	A1	19971113	WO 1997-US7702	19970506 <--

	W: AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NZ						
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
AU 9729987		A	19971126	AU 1997-29987		19970506	<--
AU 726075		B2	20001026				
ZA 9703894		A	19980223	ZA 1997-3894		19970506	<--
CN 1224427		A	19990728	CN 1997-196134		19970506	<--
BR 9708929		A	19990803	BR 1997-8929		19970506	<--
HU 9902893		A2	19991228	HU 1999-2893		19970506	<--
HU 9902893		A3	20000428				
EP 1007530		A1	20000614	EP 1997-924605		19970506	<--
EP 1007530		B1	20051116				
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI						
NZ 332320		A	20000728	NZ 1997-332320		19970506	<--
AT 310010		T	20051215	AT 1997-924605		19970506	
ES 2252784		T3	20060516	ES 1997-924605		19970506	
KR 2000010800		A	20000225	KR 1998-708934		19981106	<--
PRIORITY APPLN. INFO.:				US 1996-646477	B2	19960507	
				US 1997-841038	A	19970429	
				WO 1997-US7702	W	19970506	

OTHER SOURCE(S): MARPAT 133:17747

GI



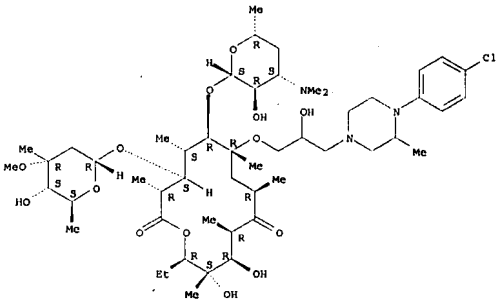
I

AB Macrolide erythromycins I (R = Me substituted with CN, F, carboxylate, sulfonate, amide, aryl, heteroaryl, substituted alkyl, alkenyl, alkynyl ;X = O, NOH, substituted oxime; R1 = H, OH; R2 = H, OH, halogen, amine, cycloalkyl, alkyl, aryl , OCONH-aryl, OCONH-heteroaryl; R3R4 = O, NOH, substituted oxime; R5 = OMe, F, OH; R6 = H, hydroxy protecting group) were prepared as antibacterial agents. Thus, I (R = allyl, R1 = R4 = OH, R2 = R3 = R6 = H, R5 = Me, X = O) was prepared and tested in vitro for its antibacterial activity (MIC = 0.01 to >100).

IT 198556-20-6P 198556-43-3P 198556-75-1P
198556-78-4P 198556-87-5P 271783-56-3P
271783-59-6P 271783-68-7P 273212-77-4P
273212-80-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-O-substituted erythromycins as antibacterial agents)

RN 198556-20-6 CAPLUS
CN Erythromycin, 6-O-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

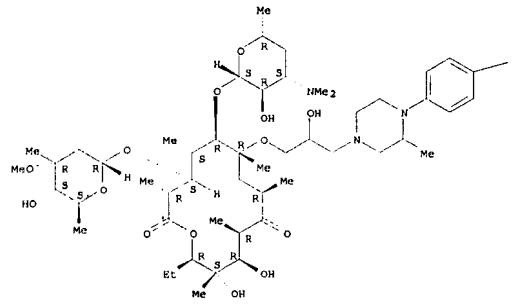
Absolute stereochemistry.



RN 198556-43-3 CAPLUS
CN Erythromycin, 6-O-[2-hydroxy-3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

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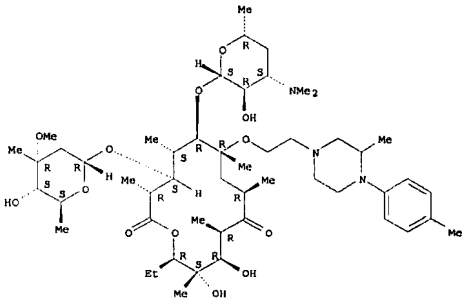
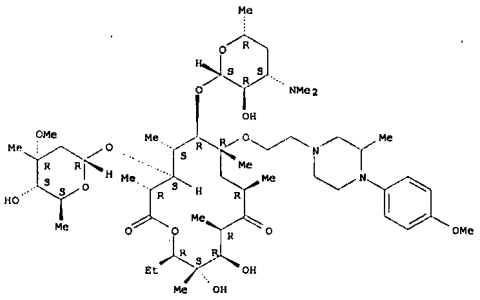
RN 198556-75-1 CAPLUS
CN Erythromycin, 6-O-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



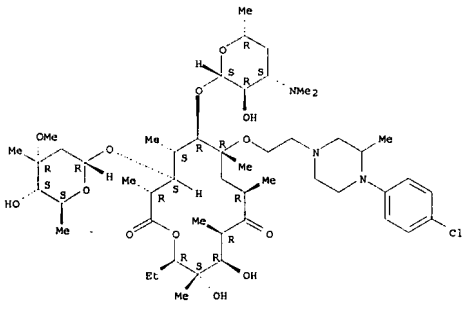
RN 198556-78-4 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



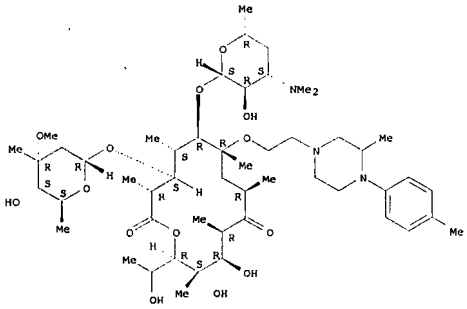
RN 198556-87-5 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



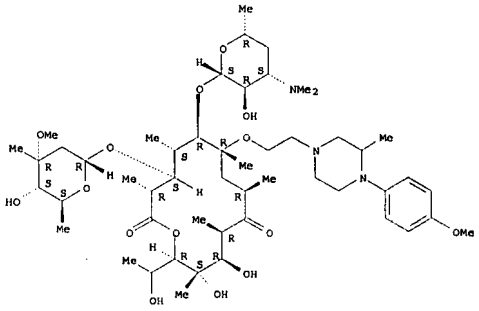
RN 271783-56-3 CAPLUS
CN Erythromycin, 14-hydroxy-6-O-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



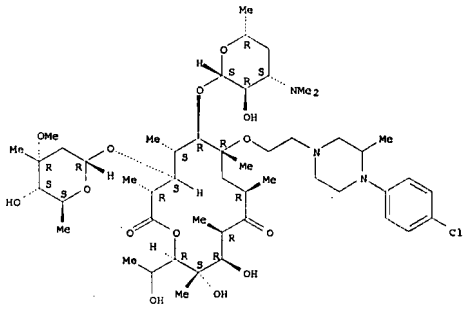
RN 271783-59-6 CAPLUS
CN Erythromycin, 14-hydroxy-6-O-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



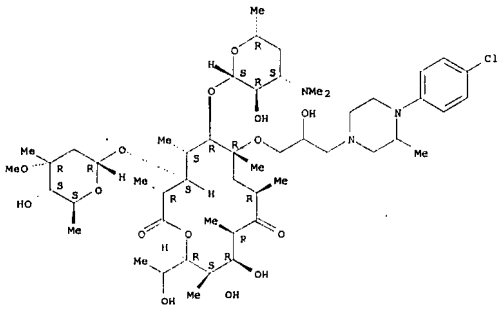
RN 271783-68-7 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-14-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 273212-77-4 CAPLUS
CN Erythromycin, 6-O-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropyl]-14-hydroxy- (9CI) (CA INDEX NAME)

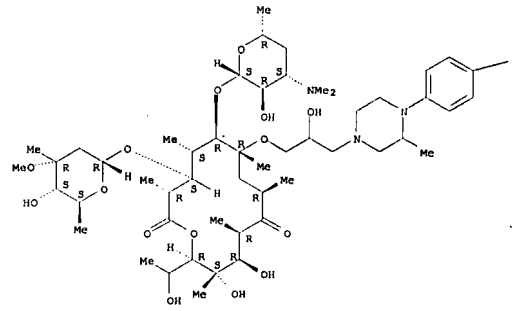
Absolute stereochemistry.



RN 273212-80-9 CAPLUS
CN Erythromycin, 14-hydroxy-6-O-[2-hydroxy-3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

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REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 26 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:241135 CAPLUS
DOCUMENT NUMBER: 132:279106
TITLE: Non-peptide GnRH agents, methods and intermediates for their preparation
INVENTOR(S): Anderson, Mark Brian; Vazir, Haresh N.; Luthin, David Robert; Paderes, Genevieve Deguzman; Pathak, Ved P.; Christie, Lance Christopher; Jiong, Yufeng; Tompkins, Eileen Valenzuela; Li, Haitao; Faust, James
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA; et al.
SOURCE: PCT Int. Appl., 444 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

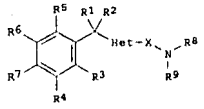
WO 2000020358	A2	20000413	WO 1999-US18790	19990820	<--
WO 2000020358	A3	20001116			
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2341346	A1	20000413	CA 1999-2341346	19990820	<--
BR 9913374	A	20010515	BR 1999-13374	19990820	<--
EP 1105120	A2	20010613	EP 1999-968010	19990820	<--
EP 1105120	B1	20050323			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
HU 200103622	A2	20020429	HU 2001-3622	19990820	<--
EE 200100102	A	20020617	EE 2001-102	19990820	<--
SI 20746	A	20020630	SI 1999-20076	19990820	<--
TR 200100631	T2	20020821	TR 2001-200100631	19990820	<--
JP 2002535244	T	20021022	JP 2000-574479	19990820	<--
AU 759310	B2	20030410	AU 2000-24709	19990820	
NZ 509252	A	20040528	NZ 1999-509252	19990820	
AT 291423	T	20050415	AT 1999-968010	19990820	
ES 2237966	T3	20050801	ES 1999-968010	19990820	
NO 20010309	A	20010411	NO 2001-309	20010119	<--
IN 2001DN00066	A	20070112	IN 2001-DN66	20010124	
ZA 2001000831	A	20020822	ZA 2001-831	20010130	<--
MX 2001PA01834	A	20000821	MX 2001-PA1834	20010219	<--
US 7101878	B1	20060905	US 2001-763216	20010220	
LV 12732	B	20020320	LV 2001-45	20010316	<--
HG 105362	A	20011231	BG 2001-105362	20010319	<--
LT 4904	B	20020425	LT 2001-24	20010319	<--
US 2004010033	A1	20040115	US 2003-353160	20030708	

PRIORITY APPLN. INFO.:

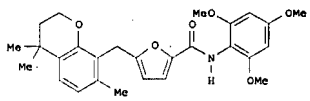
US 1998-97520P	P	19980820
WO 1999-US18790	W	19990820
US 2001-763216	B3	20010220

OTHER SOURCE(S): MARPAT 132:279106

GI



I



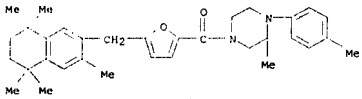
II

AB Non-peptide GnRH agents capable of inhibiting the effect of gonadotropin-releasing hormone are described. The compds. and their pharmaceutically acceptable salts, multimers, prodrugs, and active metabolites are suitable for treating mammalian reproductive disorders and steroid hormone-dependent tumors as well as for regulating fertility, where suppression of gonadotropin release is indicated. The compds. include those of formula I [X = C:O, C:S, S:O, or SO2; Het = 5-membered NOS-heterocycle; R1, R2 = H, alkyl; R3-R7 = H, halo, (un)substituted alkyl, aryl, heteroaryl, CH2OR, OR, CO2R; R = alkyl, aryl, etc.; adjacent rings positions such as R6R7 may form (un)substituted 5- or 6-membered ring with up to 4 heteroatoms; R8 = lipophilic moiety such as alkyl, aryl, CH2OR, OR, etc.; R9 = H, (un)substituted alkyl]. Methods and intermediates for synthesizing the compds. are also described. For instance, 4,4,7-trimethylchroman (preparation given) was alkylated in the 6- and 8-positions using Et 5-(chloromethyl)-2-furoate (46% total yield), and the resulting esters were hydrolyzed to a mixture of acids. This unsepd. mixture was treated with SOCl2 and amidated with 2,4,6-trimethoxyphenylamine-HCl to give the invention compound II and its chroman-6-position isomer, which were separated by HPLC. Several compds. exhibited high affinity (<100 nM) at human GnRH receptors. The compds. antagonized GnRH-stimulated inositol phosphate accumulation in cells with recombinant human GnRH receptors, and an example compound reduced plasma LH levels in castrated male rats. Various biol. data for several hundred compds. are given.

IT 263853-05-0P 263853-32-3P 263855-06-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of non-peptide GnRH agents for regulating gonadotropin secretion)

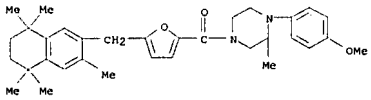
RN 263853-05-0 CAPLUS

CN Piperazine, 2-methyl-1-(4-methylphenyl)-4-[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)



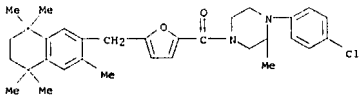
RN 263853-32-3 CAPLUS

CN Piperazine, 1-(4-methoxyphenyl)-2-methyl-4-[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)



RN 263855-06-7 CAPLUS

CN Piperazine, 1-(4-chlorophenyl)-2-methyl-4-[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 27 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:210118 CAPLUS

DOCUMENT NUMBER: 132:237107

TITLE: Preparation of piperazino-substituted cyanophenyl derivatives as antiandrogen agents

INVENTOR(S): Taniguchi, Nobuaki; Kinoyama, Isao; Kamikubo, Takashi; Toyoshima, Akira; Samizu, Kiyohiro; Kawaminami, Eiji; Imamura, Masakazu; Moritomo, Hiroyuki; Matsuhisa, Akira; Hirano, Masaaki; Miyazaki, Yoji; Nozawa, Eisuke; Okada, Minoru; Koutoku, Hiroshi; Ohta, Mitsuaki

PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan; et al.

SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

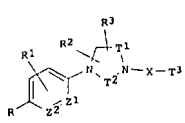
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017163	A1	20000330	WO 1999-JP5149	19990921 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2345146	A1	20000330	CA 1999-2345146	19990921 <--
AU 9956544	A1	20000410	AU 1999-56544	19990921 <--
AU 754529	B2	20021121		
BR 9914018	A	20010703	BR 1999-14018	19990921 <--
EP 1122242	A1	20010808	EP 1999-943446	19990921 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 3390744	B2	20030331	JP 2000-574073	19990921
JP 2003137873	A	20030514	JP 2002-328498	19990921
CN 1129581	B	20031203	CN 1999-811198	19990921
RU 2221785	C2	20040120	RU 2001-107612	19990921
US 6673799	B1	20040106	US 2001-787672	20010321
US 2004010037	A1	20040115	US 2003-608341	20030630

PRIORITY APPLN. INFO.:

JP 1998-267508	A	19980922
JP 1999-155398	A	19990602
JP 2000-574073	A3	19990921
WO 1999-JP5149	W	19990921
US 2001-787672	A3	20010321

OTHER SOURCE(S): MARPAT 132:237107

GI

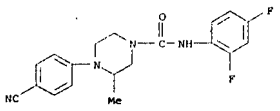


I

AB The title compds. I [T1 = (CH2)n; T2 = (CH2)k; T3 = (NR4Y)mR5; R = cyano, etc.; R1 = H, halo, etc.; R2 - R4 = H, alkyl, etc.; R5 = alkyl, etc.; k, n = 1 - 3; m = 0 or 1; X = CO, etc.; Z1, Z2 = CH, N; a proviso is given; Y = alkylene, etc.] are prepared These derivs. exhibit antiandrogen activities and are therefore useful in the prevention or treatment of prostatic cancer, prostatic hypertrophy and so forth. In an in vitro assay for inhibition of androgen binding to androgen receptors, (2R,5S)-N-(2-bromo-4-pyridyl)-4-(4-cyano-3-trifluoromethylphenyl)-2,5-dimethylpiperazine-1-carboxamide showed the Ki value of 7.5 nM.

IT 262294-07-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazino-substituted cyanophenyl derivs. as antiandrogen

agents)
RN 262294-07-5 CAPLUS
CN 1-Piperazinecarboxamide, 4-(4-cyanophenyl)-N-(2,4-difluorophenyl)-3-methyl- (9CI) (CA INDEX NAME)

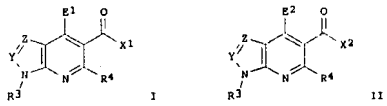


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 28 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:190924 CAPLUS
DOCUMENT NUMBER: 132:237088
TITLE: Preparation of fused pyridine inhibitors of cGMP phosphodiesterase
INVENTOR(S): Macor, John E.; Yu, Guixue
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015222	A1	20000323	WO 1999-US21070	19990913 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6326379	B1	20011204	US 1999-393833	19990910 <--
CA 2342583	A1	20000323	CA 1999-2342583	19990913 <--
AU 9961438	A1	20000403	AU 1999-61438	19990913 <--
AU 751486	B2	20020815		
EP 1113796	A1	20010711	EP 1999-948211	19990913 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

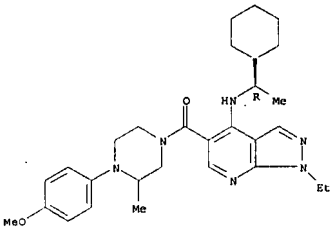
PRIORITY APPLN. INFO.: US 1998-100665P P 19980916
WO 1999-US21070 W 19990913
OTHER SOURCE(S): MARPAT 132:237088
GI



I II

AB The title compds. [I or II; E1 = OR1, SR1, NH-A1-cycloalkyl, etc.; E2 = NH-A1-alkoxy, NH-A1-CO2alkyl, NH-A1-aryl, etc.; R1 = A1-cycloalkyl, A1-alkoxy, A1-aryl, etc.; X1 = OA1R2, OR9, NR9R10, etc.; X2 = OA1R25, N(R5)A2R25, etc.; X3 = OR9, OA1OR9, NR9R10, etc.; A1 = (un)substituted alkylene; Y = N, CR6; Z = N, CR7 with the proviso that at least one of Y and Z = N; R3 = H, alkyl, cycloalkyl, etc.; R6, R7 = H, alkyl, cycloalkyl, etc.; R4 = H, 1- or 3-imidazolyl, etc.; A2 = a direct bond, alkylene, alkenyl, etc.; R2 = cycloalkyl, aryl, heteroaryl, etc.; R25 = cycloalkyl, aryl, heteroaryl, etc.; R5 = H, alkyl, cycloalkyl, etc.; R9, R10 = H, alkyl, cycloalkyl, etc.], useful for treating a cGMP PDE (especially type V) associated condition such as erectile dysfunction, were prepared Thus, reacting 4-[[(3-chloro-4-methoxyphenyl)methyl]amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid with 4-aminomethylpyridine in the presence of EDAC.HCl, 1-hydroxybenzotriazole and Et3N in THF afforded 90% II [Y = N; Z = CH; E2 = 3-Cl-4-MeOC6H3CH2NH; X2 = 4-pyridynylmethylamino; R3 = Et; R4 = H]. Compds. I are effective at 0.05-100 mg/kg/day.
IT 261770-09-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused pyridine inhibitors of cGMP phosphodiesterase)
RN 261770-09-6 CAPLUS
CN Piperazine, 4-[[4-[[(1R)-1-cyclohexylethyl]amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl]-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

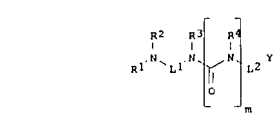


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

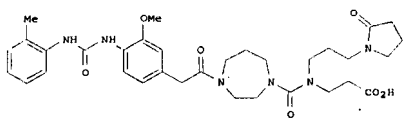
L9 ANSWER 29 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:691093 CAPLUS
DOCUMENT NUMBER: 131:310284
TITLE: Preparation of substituted diamines as α4β1 mediated cell adhesion inhibitors
INVENTOR(S): Mccarthy, Clive; Harris, Neil Victor; Morley, Andrew David
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Limited, UK
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954321	A1	19991028	WO 1999-GB1230	19990421 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937164	A	19991108	AU 1999-37164	19990421 <--

PRIORITY APPLN. INFO.: GB 1998-8431 A 19980421
GB 1998-11417 A 19980528
US 1998-104139P P 19981014
US 1998-104238P P 19981014
WO 1999-GB1230 W 19990421
OTHER SOURCE(S): MARPAT 131:310284
GI

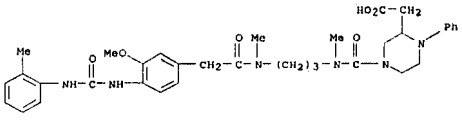


I



II

AB Substituted diamines (I) (wherein R1 = lower alkyl or various combinations of substituents, such as (cyclo)alkyl, (cyclo)alkenyl, (cyclo)alkynyl, (hetero)aryl(alkyl), etc., and linkage groups, such as C(O), C(S), (un)substituted NHC(O) or NHC(S), S(O), SO2, heteroaryldiyl, heterocycloalkylene, phenylene, etc.; R2 = H or lower alkyl; R3 and R4 = independently H or (un)substituted alkyl, alkenyl, or alkynyl; or R3 and R4 together may = (CH2)n or C(O)CH:CH; L1 = alkylene or (un)substituted (CHR10)pAr(CHR10)p; or L1N(R3) = (un)substituted alkylheterocyclo; or N(R2)L1 = (un)substituted heterocycloalkyl; or N(R2)L1N(R3) = diaza heterocyclo; L2 = (un)substituted alkylene, alkenylene, alkynylene, cycloalkenylene, cycloalkylene, or heterocycloalkylene; Y = carboxy (or an acid bioisostere) or (un)substituted C(O)NH2; Ar = phenylene, (hetero)cycloalkylene, or heteroaryldiyl; R10 = H or lower alkyl; m = 0 or 1; n = 2-4; p = 0-3] were prepd by solid phase synthesis as α4β1 mediated cell adhesion inhibitors. For example, the ureido derivative (II) was prepared using a Wang resin support. The resin was loaded with acryloyl chloride and treated sequentially with 1-(3-aminopropyl)-2-pyrrolidinone, triphosgene, homopiperazine, and 3-methoxy-4-[3-(2-methylphenyl)ureido]phenylacetic acid to yield II. Compds. of formula I regulate the interaction of VCAM-1 and fibronectin with the integrin VLA-4 (α4β1). Particular compds. of the invention suppressed cell adhesion to fibronectin and VCAM-1 with IC50 values ranging from 100μM to 1 nM in assays on metabolically labeled RAMOS cells. Particular compds. also inhibited airway inflammation after antigen challenge in mice and rats. The inhibitors caused a statistically significant reduction in eosinophil and lymphocyte nos. in bronchoalveolar lavage (BAL) and airway tissue. The invention compds., their prodrugs, pharmaceutically acceptable salts, and solvates, are useful for the treatment of inflammatory diseases and asthma.
IT 247253-69-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of substituted diamines as α4β1 mediated cell adhesion inhibitors for treatment of inflammatory diseases and asthma)
RN 247253-69-6 CAPLUS
CN 2-Piperazineacetic acid, 4-[[[3-[[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]methylamino]propyl]methylamino]carbonyl]-1-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

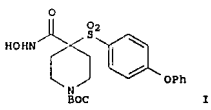
L9 ANSWER 30 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:350651 CAPLUS

DOCUMENT NUMBER: 131:18929
TITLE: Preparation of arylsulfonylheterocyclylhydroxamic acids and related compounds as matrix metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Boehm, Terri L.; De Crescenzo, Gary A.; Villamil, Clara I.; McDonald, Joseph J.; Freskos, John N.; Getman, Daniel P.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 840 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925687	A1	19990527	WO 1998-US23242	19981112 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306460	A1	19990527	CA 1998-2306460	19981112 <--
AU 9913732	A	19990607	AU 1999-13732	19981112 <--
AU 756150	B2	20030102		
BR 9814643	A	20001003	BR 1998-14643	19981112 <--
EP 1042290	A1	20001011	EP 1998-957485	19981112 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001523662	T	20011127	JP 2000-521071	19981112 <--
NZ 503485	A	20021025	NZ 1998-503485	19981112 <--
RU 2250105	C2	20050420	RU 2000-115948	19981112
ZA 9810412	A	19991209	ZA 1998-10412	19981113 <--
US 2001014688	A1	20010816	US 1998-191129	19981113 <--
NO 2000002469	A	20000712	NO 2000-2469	20000512 <--
MX 2000PA04660	A	20010930	MX 2000-PA4660	20000512 <--
US 6541489	B1	20030401	US 2000-554082	20000731
US 2002177588	A1	20021128	US 2001-954451	20010917 <--
US 6750233	B2	20040615		
US 2004048852	A1	20040311	US 2003-337942	20030107
US 6890937	B2	20050510		
US 2006084688	A1	20060420	US 2005-46645	20050128

PRIORITY APPLN. INFO.: US 1997-66007P P 19971114
US 1998-95347P P 19980804
US 1998-95501P P 19980806
US 1998-101080P P 19980918
WO 1998-US23242 W 19981112
US 1999-256948 B3 19990224
US 2000-554082 A3 20000731
US 2003-337942 A3 20030107

OTHER SOURCE(S): MARPAT 131:18929
GI



I

AB A process for treating conditions associated with pathol. matrix metalloproteinase (MMP) activity comprises administration of compds. having inhibitory activity against >1 of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibition of MMP-1. The compds. are of the form HONHCOCR1R2SO2R3 [R1, R2 = H; R1R2 = atoms to form a 5-8 membered ring containing 1-3 heteroatoms; R3 = (substituted) aryl, heteroaryl]. Thus, 4-PhOC6H4SH was heated in Me2SO to give the disulfide dimer, which in THF was added to a mixture of Et N-tert-butoxycarbonylisonipecotate (preparation given) and LDA in THF at -60° to room temperature to give 405 sulfide, which was oxidized with m-ClC6H4CO(OOH) to give 59% sulfone. The Et ester was saponified with NaOH in EtOH/H2O to give 100% acid, which in DMF was treated with hydroxybenzotriazole, EDC, 4-methylmorpholine, and aqueous NH2OH to give title compound (I). I inhibited MMP-2 with IC50 = 0.2 nM.
IT 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of arylsulfonylheterocyclylhydroxamic acids and related compds. as matrix metalloprotease inhibitors)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

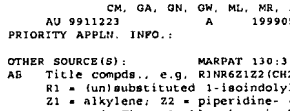
L9 ANSWER 31 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:297413 CAPLUS
DOCUMENT NUMBER: 130:311821
TITLE: Preparation of 1-[(isoindolyl- and isoquinolylamino)alkyl]-4-arylpiperazines and analogs as dopamine D4 receptor ligands
INVENTOR(S): He, Xiao-shu; De Costa, Brian; Wasley, Jan W. F.
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9921848	A2	19990506	WO 1998-US22665	19981026 <--
WO 9921848	A3	19990715		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9911223	A	19990517	AU 1999-11223	19981026 <--

PRIORITY APPLN. INFO.: US 1997-958694 A 19971027
WO 1998-US22665 W 19981026

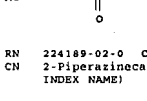
OTHER SOURCE(S): MARPAT 130:311821
AB Title compds., e.g, R1NR6Z1Z2(CH2)mR [I; R = (un)substituted (hetero)aryl; R1 = (un)substituted 1-isoindolyl, -1-isoquinolyl, etc.; R6 = H or alkyl; Z1 = alkylene; Z2 = piperidine- or piperazine-1,4-diyl; m = 0-2] were prepared Thus, 1-chloroisoquinoline was aminated by 4-(5-fluoro-2-pyrimidinyl)-1-pyrazineethylamine (preparation given) to give I (R = 5-fluoro-2-pyrimidinyl, R1 = 1-isoquinolyl, R6 = H, Z1 = CH2CH2, Z2 = piperazine-1,4-diyl). Data for biol. activity of I were given.
IT 186345-30-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study; unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-[(isoindolyl- and isoquinolylamino)alkyl]-4-arylpiperazines and analogs as dopamine D4 receptor ligands)
RN 186345-30-2 CAPLUS
CN 1H-Isoindol-3-amine, N-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]-, dihydrobromide. (9CI) (CA INDEX NAME)



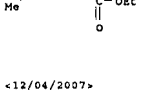
●2 HBr

L9 ANSWER 32 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:235769 CAPLUS
DOCUMENT NUMBER: 130:338083
TITLE: Hybridized and isosteric analogs of N1-acetyl-N4-dimethylpiperazinium iodide (ADMP) and N1-phenyl-N4-dimethylpiperazinium iodide (DMPP) with central nicotinic action

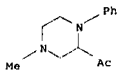
AUTHOR(S): Manetti, Dina; Bartolini, Alessandro; Borea, Pier Andrea; Bellucci, Cristina; Dei, Silvia; Ghelardini, Carla; Gualtieri, Fulvio; Romanelli, Maria Novella; Scapecchi, Serena; Teodori, Elisabetta; Varani, Katia
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy
SOURCE: Bioorganic & Medicinal Chemistry (1999), 7(3), 457-465
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of piperazine derivs., obtained by hybridization of N1-acetyl-N4-dimethylpiperazinium iodide (ADMP) and N1-phenyl-N4-dimethylpiperazinium iodide (DMPP) or of the corresponding tertiary bases with arecoline and arecolone or by isosteric substitution of the Ph ring of DMPP, has been synthesized. Hybridization afforded compds. that, both as tertiary bases and as iodomethylates, have no affinity for the nicotinic receptor. On the contrary, isosteric substitution gave compds. that maintain affinity for the receptor; among them, 1-methyl-4-(3- or 4-pyridinyl)piperazine show affinity in the nanomolar range for the nicotinic receptor. The pharmacol. profile of these isomeric compds. is quite interesting as they present differences in their peripheral and central effects, suggesting that they interact with different subtypes of the nicotinic receptor.
IT 224189-00-8P 224189-02-0P 224189-13-3P 224189-15-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(hybridized and isosteric analogs of N1-acetyl- and N1-phenyl-N4-dimethylpiperazinium iodide with central nicotinic action)
RN 224189-00-8 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-methyl-1-phenyl-, methyl ester (9CI) (CA INDEX NAME)



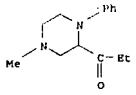
RN 224189-02-0 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-methyl-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



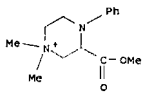
RN 224189-13-3 CAPLUS
CN Ethanone, 1-(4-methyl-1-phenyl-2-piperazinyl)- (9CI) (CA INDEX NAME)



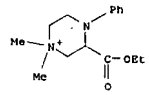
RN 224189-15-5 CAPLUS
CN 1-Propanone, 1-(4-methyl-1-phenyl-2-piperazinyl)- (9CI) (CA INDEX NAME)



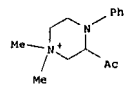
IT 224189-01-9P 224189-03-1P 224189-14-4P
224189-16-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(hybridized and isosteric analogs of N1-acetyl- and N1-phenyl-N4-dimethylpiperazinium iodide with central nicotinic action)
RN 224189-01-9 CAPLUS
CN Piperazinium, 3-(methoxycarbonyl)-1,1-dimethyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



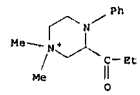
RN 224189-03-1 CAPLUS
CN Piperazinium, 3-(ethoxycarbonyl)-1,1-dimethyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



RN 224189-14-4 CAPLUS
CN Piperazinium, 3-acetyl-1,1-dimethyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



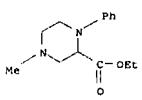
RN 224189-16-6 CAPLUS
CN Piperazinium, 1,1-dimethyl-3-(1-oxopropyl)-4-phenyl-, iodide (9CI) (CA INDEX NAME)



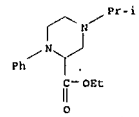
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 33 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:234565 CAPLUS
DOCUMENT NUMBER: 131:18981
TITLE: Design and Synthesis of Imidazoline Derivatives Active on Glucose Homeostasis in a Rat Model of Type II Diabetes. 2. Syntheses and Biological Activities of 1,4-Dialkyl-, 1,4-Dibenzyl, and 1-Benzyl-4-alkyl-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazines and

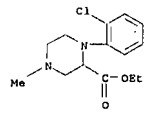
Isosteric Analogs of Imidazoline
AUTHOR(S): Le Bihan, Gaeelle; Rondu, Frederic; Pele-Tounian, Agnes; Wang, Xuan; Lidy, Sandrine; Touboul, Estera; Lamouri, Aazdine; Dive, Georges; Huet, Jack; Pfeiffer, Bruno; Renard, Pierre; Guardiola-Lemaitre, Beatrice; Manechez, Dominique; Penicaud, Luc; Ktorza, Alain; Godfroid, Jean-Jacques
CORPORATE SOURCE: Laboratoire de Pharmacochimie Moleculaire et Systemes Membranaires, Universite Paris 7-Denis Diderot, Paris, 75251, Fr.
SOURCE: Journal of Medicinal Chemistry (1999), 42(9), 1587-1603
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Piperazine deriva. were identified as new antidiabetic compds. Structure-activity relationship studies in a series of 1-benzyl-4-alkyl-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazines resulted in the identification of 1-methyl-4-(2',4'-dichlorobenzyl)-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazine, PMS 812 (S-21663), as a highly potent antidiabetic agent on a rat model of diabetes, mediated by an important increase of insulin secretion independently of α2-adrenoceptor blockage. These studies were extended to find addnl. compds. in these series with improved properties. In such a way, substitution of both piperazine N atoms was first optimized by using various alkyl, branched or not, and benzyl groups. Second, some modifications of the imidazoline ring and its replacement by isosteric heterocycles were carried out, proceeding from PMS 812, to evaluate their influence on the antidiabetic activity. The importance of the distance between the imidazoline ring and the piperazine skeleton was studied third. Finally, the influence of the N-benzyl moiety was also analyzed compared to a direct N-Ph substitution. The pharmacol. evaluation was performed in vivo using glucose tolerance tests on a rat model of type II diabetes. The most active compds. were 1,4-diisopropyl-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazine, PMS 847 (S-22068), and 1,4-diisobutyl-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazine, PMS 889 (S-22575), which strongly improved glucose tolerance without any side event or hypoglycemic effect. More particularly, PMS 847 proved to be as potent after po (100 μmol/kg) as after i.p. administration and appears as a good candidate for clin. investigations.
IT 224189-02-0P 226068-23-1P 226068-29-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antidiabetic activity of and (benzyl)(alkyl)(imidazolyl)piperazines and isosteric analogs)
RN 224189-02-0 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-methyl-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 226068-23-1 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-(1-methylethyl)-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

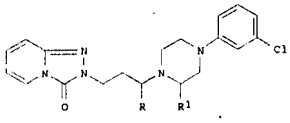


RN 226068-29-7 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-(2-chlorophenyl)-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 34 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:89740 CAPLUS
DOCUMENT NUMBER: 130:209646
TITLE: Effect of Modifications of the Alkylpiperazine Moiety of Trazodone on 5HT2A and σ1 Receptor Binding Affinity
AUTHOR(S): Giannangeli, Marilena; Cazzolla, Nicola; Luparini, Maria Rita; Magnani, Maurizio; Mabilia, Massimo; Picconi, Giuseppe; Tomaselli, Mauro; Baiocchi, Leandro
CORPORATE SOURCE: Department of Medicinal Chemistry, Angelini Ricerche S.p.A., S. Palomba-Pomezia, 00040, Italy
SOURCE: Journal of Medicinal Chemistry (1999), 42(1), 336-345
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



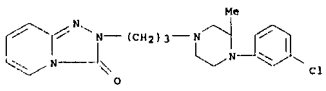
I

AB A series of triazolopyridine deriva. were synthesized in order to explore the effect of modifications of the alkylpiperazine moiety of trazodone on binding affinity for 5HT2A and α1 receptors. All of the synthesized compds. show a decrease of affinity for both 5HT2A and α1 receptors, as compared to trazodone, with the exception of I [R = Me, R1 = H; R = H, R1 = Me]. These compds. showed a decrease of affinity only for the α1 receptor. The stereochem. influence of the piperazine moiety of I [R = H, R1 = Me] was also evaluated. Enantiomer (S)-I [R = H, R1 = Me] showed the most significant differences between 5HT2A and α1 receptor affinity (IC50 values) and among the corresponding functional properties (pA2 values). Since (S)-I [R = H, R1 = Me] cannot generate the metabolite 4-(3-chlorophenyl)piperazine this product was selected for further pharmacol. studies.

IT 151448-02-1P 220909-95-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(effect of modifications of the alkylpiperazine moiety of Trazodone on 5HT2A and α1 receptor binding affinity)

RN 151448-02-1 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



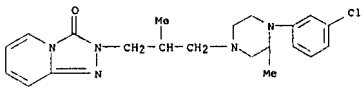
● HCl

RN 220909-95-5 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]-2-methylpropyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

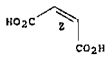
CRN 220909-94-4
CMF C21 H26 Cl N5 O



CM 2

CRN 110-16-7
CMF C4 H4 O4

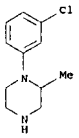
Double bond geometry as shown.



IT 75348-33-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(effect of modifications of the alkylpiperazine moiety of Trazodone on 5HT2A and α1 receptor binding affinity)

RN 75348-33-3 CAPLUS

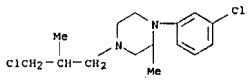
CN Piperazine, 1-(3-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



IT 220909-98-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(effect of modifications of the alkylpiperazine moiety of Trazodone on 5HT2A and α1 receptor binding affinity)

RN 220909-98-8 CAPLUS

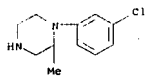
CN Piperazine, 4-(3-chloro-2-methylpropyl)-1-(3-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



IT 220910-03-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(effect of modifications of the alkylpiperazine moiety of Trazodone on 5HT2A and α1 receptor binding affinity)

RN 220910-03-2 CAPLUS

CN Piperazine, 1-(3-chlorophenyl)-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



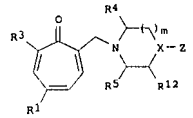
● HCl

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

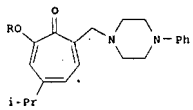
L9 ANSWER 35 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:34895 CAPLUS
DOCUMENT NUMBER: 130:95566
TITLE: Preparation of tropone derivatives for remedies/preventives for frequent urination/urinary incontinence
INVENTOR(S): Koga, Ichiro; Narita, Kazuhisa; Okada, Atsushi
PATENT ASSIGNEE(S): Nippon Kayaku Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900366	A1	19990107	WO 1998-JP2865	19980626 <--
W: AU, CA, CN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2294312	A1	19990107	CA 1998-2294312	19980626 <--
AU 9879341	A	19990119	AU 1998-79341	19980626 <--
AU 736510	B2	20010726		
EP 995741	A1	20000426	EP 1998-929705	19980626 <--
R: AT, CH, DE, FR, GB, IT, LI, SE				
US 6221868	B1	20010424	US 1999-446423	19991220 <--
PRIORITY APPLN. INFO.:			JP 1997-186030 A	19970627
			JP 1997-225552 A	19970808
			JP 1997-256223 A	19970905
			WO 1998-JP2865 W	19980626

OTHER SOURCE(S): MARPAT 130:95566
GI



I



II

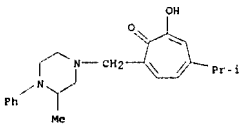
AB Claimed are remedies/preventives for frequent urination/urinary incontinence which contain as the active ingredient compds. having a tropone skeleton or pharmacol. acceptable salts thereof and novel compds. having the tropone skeleton. The compds. having a tropone skeleton and showing the above pharmacol. effects are those represented by, for example, general formula [I; R1, R2 = hydrogen, (un)substituted lower alkyl or aryl; R3 = OR6 or NR7R8; wherein R6 = H, (un)substituted lower alkyl, aralkyl, or acyl; R7, R8 = H, optionally heteroatom-substituted lower alkyl, (un)substituted aralkyl; or R7 and R8 together represent a 5- to 10-membered ring optionally containing O or NR9; wherein R9 = H, (un)substituted lower alkyl or aryl; R4 , R5 = H, lower alkyl; R12 = H, lower alkyl; X = N, CH; Z = CH(Ar1)(Ar2), (un)substituted Ph, CH2Ph, benzoyl, 2-pyridyl, or 2-pyrimidinyl; Ar1, Ar2 = (un)substituted aryl; m = 1,2]. These compds. increase bladder volume and prolong urination intervals by inhibiting urination reflex, does not exhibit the side effects of anticholinergic agents such as dry mouth and iachuria (retention of urine), and are effective for patients in whom increase in atropine-resistant contraction are noticed. Thus, 37% aqueous formalin solution was added to a solution of 8.2 g hinokitiol, 7.8 mL 1-phenylpiperazine, and 2.9 mL AcOH in 5 mL MeOH and heated at 60° fro 2.5 h to give 7-(4-phenylpiperazinomethyl)-2,4,6-cycloheptatrien-1-one derivative (II; R = H), which was ethylated by di-Et sulfate in the presence of K2CO3 in acetone under reflux for 6 h to give II (R = Et). II (R = H) and II (R = Et) at 5 mg/kg i.v. prolonged the ratio of interval of rat rhythmic bladder contraction before and after the administration of the compds. by the factor of 12.7 and 22.3, resp.

IT 219145-21-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tropone derivs. for remedies/preventives for frequent urination/urinary incontinence)

RN 219145-21-8 CAPLUS

CN 2,4,6-Cycloheptatrien-1-one, 2-hydroxy-4-(1-methylethyl)-7-[(3-methyl-4-

phenyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



IT 2946-76-1P, 2-Methyl-1-phenylpiperazine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tropone derivs. for remedies/preventives for frequent urination/urinary incontinence)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

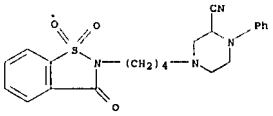
L9 ANSWER 36 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:604657 CAPLUS
DOCUMENT NUMBER: 129:245169
TITLE: Preparation of 1,4-disubstituted piperazines as alpha 1a adrenergic receptor antagonists
INVENTOR(S): Bock, Marg G.; Patane, Michael A.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5807856	A	19980915	US 1996-747687	19961112 <--
PRIORITY APPLN. INFO.:			US 1996-747687	19961112
OTHER SOURCE(S):	MARPAT 129:245169			

GI

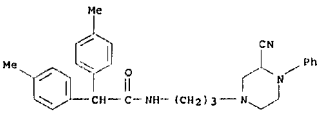
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I or II; W = (un)substituted Ph, pyridyl, thienyl, etc.; R1, R2 = CN, CONR4R5, CO2R4, SO2R4; R3 = III; R4, R5 = H, C1-8 alkyl, C3-8 cycloalkyl; R7 = C1-8 alkyl, iso-Pr, (un)substituted Ph, etc.; T, U, X, Y, Z = H, halo, C1-8 alkyl, etc.; n = 2-6], useful as selective alpha 1a adrenergic receptor antagonists in treating benign prostatic hyperplasia, were prepared Thus, reaction of piperazine IV.HCl with amide V in the presence of iPr2NEt in DMF afforded the title compound VI. Representative compds. I and II showed Ki of ≤300 nM against alpha 1a adrenergic receptor binding. Compds. I and II are selective in their ability to relax smooth muscle tissue enriched in the alpha 1a receptor subtype without at the same time inducing orthostatic hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the instant compds. is to provide acute relief to males suffering from benign prostatic hyperplasia, by permitting less hindered urine flow. Another utility of the instant compds. is provided by combination with a human 5-alpha reductase inhibitory compound, such that both acute and chronic relief from the effects of benign prostatic hyperplasia are achieved.
IT 191156-62-4P 191156-63-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,4-disubstituted piperazines as alpha 1a adrenergic receptor antagonists)
RN 191156-62-4 CAPLUS
CN 2-Piperazinecarbonitrile, 4-[4-(1,1-dioxido-3-oxo-1,2-benzisothiazol-2(3H)-yl)butyl]-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



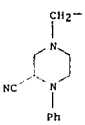
● HCl

RN 191156-63-5 CAPLUS
CN Benzeneacetamide, N-[3-(3-cyano-4-phenyl-1-piperazinyl)propyl]-4-methyl-α-(4-methylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT 135036-22-5P 191156-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1,4-disubstituted piperazines as alpha 1a adrenergic receptor antagonists)
RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 191156-64-6 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

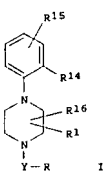
● HCl

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 37 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:352630 CAPLUS
DOCUMENT NUMBER: 129:27960
TITLE: Preparation of piperazine derivatives as tocolytic oxytocin receptor antagonists
INVENTOR(S): Bock, Mark G.; Evans, Ben E.; Culberson, J. Christopher; Gilbert, Kevin F.; Rittle, Kenneth E.; Williams, Peter D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. 5,464,788.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

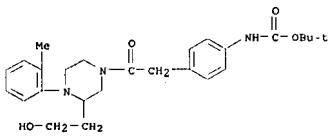
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5756504	A	19980526	US 1996-718415	19960923 <--
US 5464788	A	19951107	US 1994-217270	19940324 <--
WO 9525443	A1	19950928	WO 1995-US3738	19950323 <--
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1994-217270	A2 19940324
			WO 1995-US3738	W 19950323
OTHER SOURCE(S):	MARPAT 129:27960			

GI

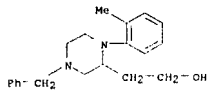


AB The title compds. I [Y = SO2, (CH2)pCO(CH2)p, etc.; p = 1-3; R = (un)substituted Ph, etc.; R1 = H, cyano, Ph, CONHR2, CONR2R2, etc.; R2 = H, C3-8 cycloalkyl or C1-5 alkyl; R14, R15 = C1-5 alkyl or alkoxy, halo; R16 = H or oxo] were prepared I are useful as oxytocin and vasopressin receptor antagonists. Thus, spiro[1H]indene-1,4'-piperidine.HCl was treated with 2,4-dimethoxy-phenylacetic acid in the presence of EDC, HBT and Et3N to give 1'-(2,4-dimethoxyphenylacetyl)-spiro[1H]indene-1,4'-piperidine, which showed IC50 of 400 nM for [3H]oxytocin.
IT 170929-79-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine derivs. as tocolytic oxytocin receptor

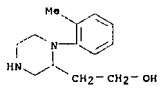
antagonists)
RN 170929-79-0 CAPLUS
CN Carbamic acid, [4-[2-[3-(2-hydroxyethyl)-4-(2-methylphenyl)-1-piperazinyl]-2-oxoethyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT 170930-08-2P 170930-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazine derivs. as tocolytic oxytocin receptor antagonists)
RN 170930-08-2 CAPLUS
CN 2-Piperazineethanol, 1-(2-methylphenyl)-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 170930-09-3 CAPLUS
CN 2-Piperazineethanol, 1-(2-methylphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

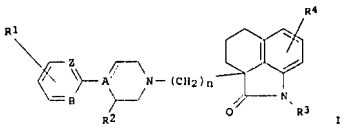
L9 ANSWER 38 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:55616 CAPLUS
DOCUMENT NUMBER: 128:114961
TITLE: Preparation of tetrahydrobenzindole derivatives for the treatment or prevention of mental diseases
INVENTOR(S): Koyama, Masao; Kikuchi, Chika; Ushiroda, Osamu; Ando, Takashi; Nagaso, Hiroshi; Fuji, Kazuyuki; Okuno,

Masayo; Hiranuma, Toyokazu
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800400	A1	19980108	WO 1997-JP2226	19970627 <--
W: CA, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2259218	A1	19980108	CA 1997-2259218	19970627 <--
CA 2259218	C	20060725		
EP 937715	A1	19990825	EP 1997-928490	19970627 <--
EP 937715	B1	20050601		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 296801	T	20050615	AT 1997-928490	19970627
ES 2243999	T3	20051201	ES 1997-928490	19970627
NO 9806141	A	19990217	NO 1998-6141	19981228 <--
NO 311515	B1	20011203		
US 6355642	B1	20020312	US 1998-214114	19981228 <--

PRIORITY APPLN. INFO.: JP 1996-169702 A 19960628
JP 1997-96271 A 19970415
JP 1997-130201 A 19970521
JP 1997-144376 A 19970603
WO 1997-JP2226 W 19970627

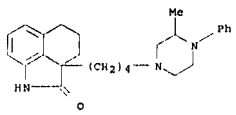
OTHER SOURCE(S): MARPAT 128:114961
GI



I

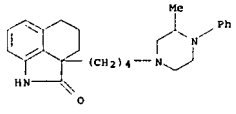
AB The title compds. I [A represents N, CH, C having a double bond or CR5; B and Z independently represent each N, CH or CR1, provided that A is N when B and/or Z is N; R1 represents hydrogen, halogeno, lower alkyl, cyano, trihalomethyl, hydroxy, alkoxy, alkylthio, alkylsulfenyl, alkylsulfonyl, alkoxycarbonyl, sulfamoyl, optionally substituted amino, optionally alkylated carbamoyl, acyl or carboxy; R2 represents hydrogen or lower alkyl; R3 represents hydrogen, lower alkyl; R3 represents hydrogen, lower alkyl or aralkyl; R4 represents hydrogen, halogeno, lower alkyl, hydroxyl, alkoxy, acyl, alkoxycarbonyl, nitro, optionally substituted amino, optionally alkylated carbamoyl or acyloxy; R5 represents lower alkyl, cyano, carbamoyl, carboxy, acyl, acyloxy, alkoxy, alkoxycarbonyl,

trihalomethyl or hydroxy; and n is an integer of from 2 to 6] are prepared 1 strongly inhibit [3H]-serotonin and [3H]-5-CT binding to the human serotonin 5-HT7 receptor subtype expressed in a cultured cell line and are useful for treating or preventing mental diseases. 2A-[4-[4-(2-Methoxyphenyl)piperazinyl]butyl]-2a,3,4,5-tetrahydrobenz[cd]indol-2-(1H)-one was prepared from 2a,3,4,5-tetrahydrobenz[cd]indol-2-(1H)-one. In tests for affinity for the 5-HT7 receptors, compds. of this invention showed Ki values of 8.9 nM to 27 nM. The title compds. showed selective affinity for 5-HT7 receptors.
IT 201608-75-5P 201608-76-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tetrahydrobenzindole derivs. for treatment or prevention of mental diseases)
RN 201608-75-5 CAPLUS
CN Benz[cd]indol-2(1H)-one, 2a,3,4,5-tetrahydro-2a-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]-, monohydrochloride (9CI) (CA INDEX NAME)

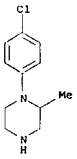


● HCl

RN 201608-76-6 CAPLUS
CN Benz[cd]indol-2(1H)-one, 2a,3,4,5-tetrahydro-2a-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)

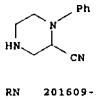


IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of tetrahydrobenzindole derivs. for treatment or prevention of mental diseases)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)

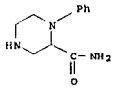


IT 2946-76-1P 201609-32-7P 201609-33-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tetrahydrobenzindole derivs. for treatment or prevention of mental diseases)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 201609-32-7 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl- (9CI) (CA INDEX NAME)



RN 201609-33-8 CAPLUS
CN 2-Piperazinecarboxamide, 1-phenyl- (9CI) (CA INDEX NAME)



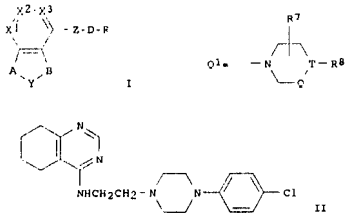
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 39 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:13943 CAPLUS

DOCUMENT NUMBER: 128:61522
TITLE: Preparation of fused heterocyclic compounds as antagonists of D2 and D4 receptors
INVENTOR(S): Kuroita, Takanobu; Togo, Yoshifumi; Ishibuchi, Seigo; Fujio, Masakazu; Futamura, Takashi
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9747601	A1	19971218	WO 1997-JP1993	19970609 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9729807	A	19980107	AU 1997-29807	19970609 <--
JP 3531169	B2	20040524	JP 1998-501435	19970609
PRIORITY APPLN. INFO.:			JP 1996-149620 A	19960611
			WO 1997-JP1993 W	19970609

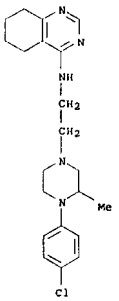
OTHER SOURCE(S): MARPAT 128:61522
GI



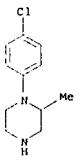
AB Fused heterocyclic compds. represented by general formula [I; X1-X2-X3 = NCR1N, CR1CR2N, NCR1CR2, CR1NCR2, NNCR1; R1, R2 = H, alkyl, OH, NH2, arylalkyl, (un)substituted aryl or heteroaryl; A = linear or branched and (un)substituted C1-4 alkyl; Y = O, S, SO, SO2, (un)substituted NH; B = linear or branched alkyl and (un)substituted C1-4 alkylene; Z = O, S, SO, SO2, (un)substituted NH, CH(OH), CO, CH2; D = linear or branched alkyl

C1-8 alkylene; R = heterocyclyl, e.g., Q1; wherein Q-T = (CH2)n, CH2CH, CH:C; wherein R7 = H, alkyl; R8 = (un)substituted aromatic hydrocarbyl or heterocyclyl) or optical isomers or pharmaceutically acceptable salts thereof are prepared. Also claimed are medicinal compns. comprising these compds. and pharmaceutically acceptable additives, and drugs comprising these compds. These compds. exert more potent blocking effects on D4 receptors than on D2 receptors. Moreover, they have high affinities for receptors other than dopamine receptors such as muscarine M1, and serotonin-2 (5-HT2) and adrenalin α1 and α2 receptors. Thus, these compds. are efficacious against not only pos. symptoms typified by hallucination and delusion characteristic of the acute stage of schizophrenia but also neg. symptoms such as emotional torpidity, abulia, and autism. In addition, they are useful as antipsychotic agents with relieved side effects such as extrapyramidal symptoms and abnormal internal secretion observed in association with the administration of the conventional antipsychotic agents having only D2 receptor antagonism. The above compds. are usable as remedies for diseases such as schizophrenia. Thus, N-(5,6,7,8-tetrahydroquinazolin-4-yl)-2-chloroacetamide (preparation given) and N-(4-chlorophenyl)piperazine hydrochloride were dissolved in DMF and stirred with K2CO3 and KI at room temperature for 24 h to give N-(5,6,7,8-tetrahydroquinazolin-4-yl)-2-[4-(4-chlorophenyl)piperazin-1-yl]acetamide, which was reduced by LiAlH4 in THF at room temperature for 30 min to give the title compound (II). II and another compound tested in vitro showed affinity for D2 and D4 receptors of nerve synapses membrane with Ki value of 25 nM and 0.01-1 nM, resp.

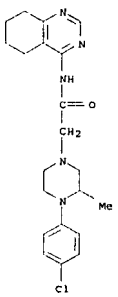
IT 200412-33-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused heterocyclic compds. having antagonism for D2 and D4 receptors as antipsychotics)
RN 200412-33-5 CAPLUS
CN 4-Quinazolinamine, N-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fused heterocyclic compds. having antagonism for D2 and D4 receptors as antipsychotics)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



IT 200413-37-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of fused heterocyclic compds. having antagonism for D2 and D4 receptors as antipsychotics)
RN 200413-37-2 CAPLUS
CN 1-Piperazineacetamide, 4-(4-chlorophenyl)-3-methyl-N-(5,6,7,8-tetrahydro-4-quinazolinyl)- (9CI) (CA INDEX NAME)

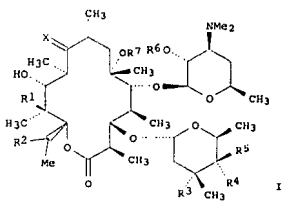


L9 ANSWER 40 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:746060 CAPLUS

DOCUMENT NUMBER: 127:359051
TITLE: Preparation of 6-O-substituted erythromycins as bactericides
INVENTOR(S): Or, Yat Sun; Clark, Richard F.; Ma, Zhenkun; Griesgraber, George; Li, Leping; Chu, Daniel T.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9742206	A1	19971113	WO 1997-US7702	19970506 <--
W: AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6075011	A	20000613	US 1997-841038	19970429 <--
CA 2253330	A1	19971113	CA 1997-2253330	19970506 <--
CA 2253330	C	20060725		
AU 9729987	A	19971126	AU 1997-29987	19970506 <--
AU 726075	B2	20001026		
BR 9708929	A	19990803	BR 1997-8929	19970506 <--
EP 1007530	A1	20000614	EP 1997-924605	19970506 <--
EP 1007530	B1	20051116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
NZ 332320	A	20000728	NZ 1997-332320	19970506 <--
JP 2002515034	T	20020521	JP 1997-540164	19970506
AT 310010	T	20051215	AT 1997-924605	19970506
PRIORITY APPLN. INFO.:			US 1996-646477 A	19960507
			US 1997-841038 A	19970429
			WO 1997-US7702 W	19970506

OTHER SOURCE(S): MARPAT 127:359051
GI



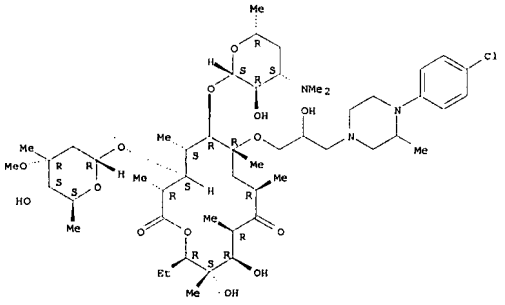
AB Antimicrobial erythromycins, e.g. I (X = O, NOH, NOR; R = alkyl, aralkyl, cycloalkyl, arylsilyl; R1, R2 = H, OH; R3 = OMe, F, OH; R4, R5 = one is H and the other is OH, alkyl, aralkyl, sulfone; R4, R5 = X; R6 = H, hydroxy protecting group; R7 = F, alkyl, alkenyl, alkynyl sulfone, amide), were

prepared as bactericides. Thus, I (X = O; R1 = R4= OH; R2 = R5 = R6 = H; R3 = OMe, R7 = Pr) was prepared and tested for its in vitro antibacterial activity (MIC = 0.05-100).

IT 198556-20-6P 198556-43-3P 198556-75-1P
198556-78-4P 198556-87-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 6-O-substituted erythromycins as bactericides)

RN 198556-20-6 CAPLUS
CN Erythromycin, 6-O-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

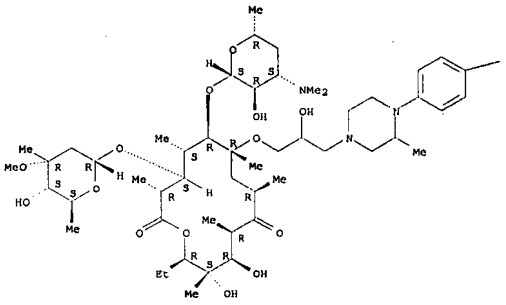
Absolute stereochemistry.



RN 198556-43-3 CAPLUS
CN Erythromycin, 6-O-[2-hydroxy-3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

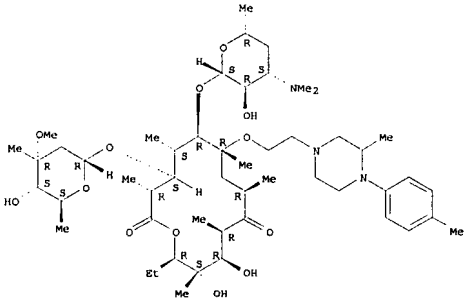


PAGE 1-B

OMe

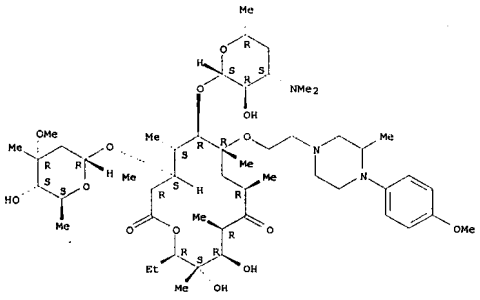
RN 198556-75-1 CAPLUS
CN Erythromycin, 6-O-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



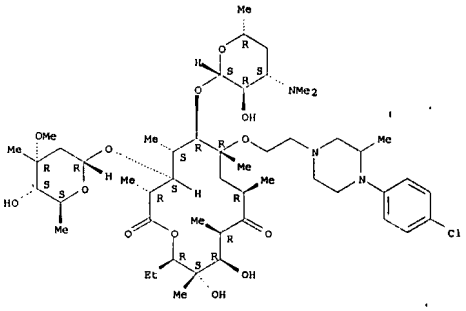
RN 198556-78-4 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 198556-87-5 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



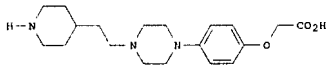
L9 ANSWER 41 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:684389 CAPLUS
DOCUMENT NUMBER: 127:358876
TITLE: Preparation of heterocyclylphenoxyalkanoates and analogs as cell aggregation inhibitors
INVENTOR(S): Pieper, Helmut; Linz, Gunter; Austel, Volkhard; Himmelsbach, Frank; Guth, Brian; Weisenberger, Johannes
PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H., Germany
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9737975	A1	19971016	WO 1997-EP1698	19970404 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19614204	A1	19971016	DE 1996-19614204	19960410 <--
US 5994356	A	19991130	US 1997-832259	19970403 <--
CA 2244860	A1	19971016	CA 1997-2244860	19970404 <--
AU 9726368	A	19971029	AU 1997-26368	19970404 <--
EP 892783	A1	19990127	EP 1997-918113	19970404 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI

JP 2000508307	T	20000704	JP 1997-535832		19970404 <--
ZA 9703002	A	19981009	ZA 1997-3002		19970409 <--
PRIORITY APPLN. INFO.:			DE 1996-19614204	A	19960410
			WO 1997-EP1698	W	19970404

OTHER SOURCE(S): MARPAT 127:358876
GI

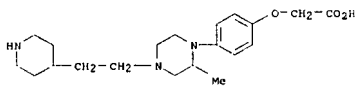


II

AB R1Z1Z2Z3Z4Z5R [I; R = OH, alkoxy, OPh, etc.; R1 = H, (phenyl)alkyl, etc.; Z1 = (oxo)piperazine-1,4-diyl, (oxo)piperidine-1,4-diyl; Z2 = CH2CH2, COCH2, NHCO, CO2, etc.; Z3 = (un)substituted (oxo)piperazine-1,4-diyl, -(oxo)piperidine-1,4- or 4,1-diyl, ,-cyclohexylene, etc.; Z4 = piperidinediyl, phenylene, cyclohexylene, etc.; Z5 = OCH2CO, NHCH2CO, CH2CO, etc.] were prepared Thus, Me 4-piperazinophenoxyacetate was N-alkylated by 2-(1-tert-butoxycarbonyl-4-piperidinyl)ethyl methanesulfonate and the product converted in 2 steps to title compound II.2HCl. Data for biol. activity of I were given.

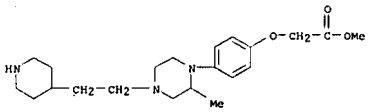
IT 198626-02-7P 198626-25-4P 198626-78-7P
198627-21-3P 198627-41-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclylphenoxyalkanoates and analogs as cell aggregation inhibitors)

RN 198626-02-7 CAPLUS
CN Acetic acid, [4-[2-methyl-4-[2-(4-piperidinyl)ethyl]-1-piperazinyl]phenoxy]-, dihydrochloride (9CI) (CA INDEX NAME)



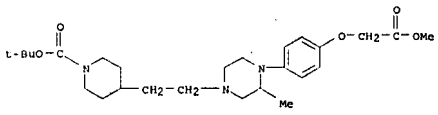
●2 HCl

RN 198626-25-4 CAPLUS
CN Acetic acid, [4-[2-methyl-4-[2-(4-piperidinyl)ethyl]-1-piperazinyl]phenoxy]-, methyl ester, dihydrochloride (9CI) (CA INDEX NAME)

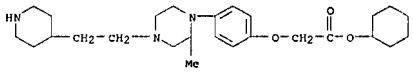


●2 HCl

RN 198626-78-7 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[2-[4-[4-(2-methoxy-2-oxoethoxy)phenyl]-3-methyl-1-piperazinyl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

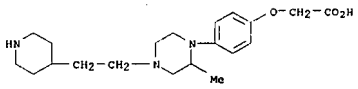


RN 198627-21-3 CAPLUS
CN Acetic acid, [4-[2-methyl-4-[2-(4-piperidinyl)ethyl]-1-piperazinyl]phenoxy]-, cyclohexyl ester, dihydrochloride (9CI) (CA INDEX NAME)



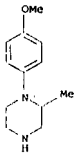
●2 HCl

RN 198627-41-7 CAPLUS
CN Acetic acid, [4-[2-methyl-4-[2-(4-piperidinyl)ethyl]-1-piperazinyl]phenoxy]- (9CI) (CA INDEX NAME)



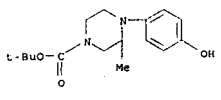
IT 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclylphenoxyalkanoates and analogs as cell aggregation inhibitors)

RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

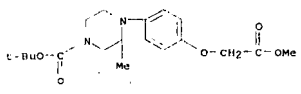


IT 198627-59-7P 198627-60-0P 198627-62-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclylphenoxyalkanoates and analogs as cell aggregation inhibitors)

RN 198627-59-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(4-hydroxyphenyl)-3-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



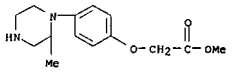
RN 198627-60-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-(2-methoxy-2-oxoethoxy)phenyl]-3-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 198627-62-2 CAPLUS
CN Acetic acid, [4-(2-methyl-1-piperazinyl)phenoxy]-, methyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 198627-61-1
CMF C14 H20 N2 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

L9 ANSWER 42 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:456780 CAPLUS
DOCUMENT NUMBER: 127:50667
TITLE: Preparation of piperazine derivatives as alpha 1a adrenergic receptor antagonists
INVENTOR(S): Bock, Mark G.; Patane, Michael A.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Bock, Mark G.; Patane, Michael A.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9718209	A1	19970522	WO 1996-US18346	19961112 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9677344	A	19970605	AU 1996-77344	19961112 <--
PRIORITY APPLN. INFO.:			US 1995-7964P	P 19951115
			GB 1996-5165	A 19960312
			WO 1996-US18346	W 19961112

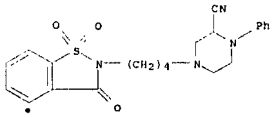
OTHER SOURCE(S): MARPAT 127:50667
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; W = (un)substituted Ph, pyridyl, thienyl, etc.; R1, R2 = H, CN, CHNR4R5, CO2R4, SO2R4 (wherein R4, R5 = H, C1-8 alkyl, C3-8 cycloalkyl); R3 = II, III (wherein R6 = H, Cl; R7 = C1-8 alkyl, etc.; T, U, X, Y, Z = H, halo, C1-8 alkyl, C3-8 cycloalkyl, etc.; n = 2-6)] and their salts, selective alpha 1a adrenergic receptor antagonists and useful in the treatment of benign prostatic hyperplasia, were prepared Thus, reaction of 2-cyano-1-phenylpiperazine with 4-bromobutylsaccharin in the presence of EtN(iPr)2 in DMF afforded IV.HCl which Ki of ≤ 300 nM against alpha 1a adrenergic receptor binding. Compds. I are selective in their ability to relax smooth muscle tissue enriched in the alpha 1a receptor subtype without at the same time inducing orthostatic hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the instant compds. is to provide acute relief to males suffering from benign prostatic hyperplasia, by permitting less hindered urine flow. Another utility of the instant compds. is provided by combination with a human 5-alpha reductase inhibitory compound, such that both acute and chronic relief from the effects of benign prostatic hyperplasia are achieved.

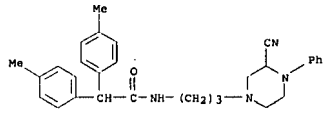
IT 191156-62-4P 191156-63-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine derivs. as alpha 1a adrenergic receptor antagonists)

RN 191156-62-4 CAPLUS
CN 2-Piperazinecarbonitrile, 4-[4-(1,1-dioxido-3-oxo-1,2-benzisothiazol-2(3H)-yl)butyl]-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

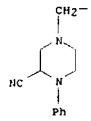
RN 191156-63-5 CAPLUS
CN Benzeneacetamide, N-[3-(3-cyano-4-phenyl-1-piperazinyl)propyl]-4-methyl-α-(4-methylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT 135036-22-5P 191156-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazine derivs. as alpha 1a adrenergic receptor antagonists)

RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 191156-64-6 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

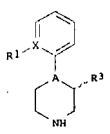
L9 ANSWER 43 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:443299 CAPLUS
DOCUMENT NUMBER: 127:65787
TITLE: Preparation of piperazine and piperidine derivatives as alpha 1a adrenergic receptor antagonists
INVENTOR(S): Bock, Mark G.; Patane, Michael A.; Ponticello, Rose

Ann
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Bock, Mark G.; Patane, Michael A.; Ponticello, Rose Ann
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9717967	A1	19970522	WO 1996-US18321	19961112 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2235370	A1	19970522	CA 1996-2235370	19961112 <--
AU 9677343	A	19970605	AU 1996-77343	19961112 <--
AU 710337	B2	19990916		
EP 865280	A1	19980923	EP 1996-940465	19961112 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11507395	T	19990629	JP 1996-519091	19961112 <--
US 5922722	A	19990713	US 1998-66477	19980422 <--

PRIORITY APPLN. INFO.: US 1995-6765P P 19951115
GB 1996-3423 A 19960219
WO 1996-US18321 W 19961112

OTHER SOURCE(S): MARPAT 127:65787
GI



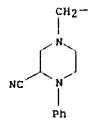
I

AB I [A = CR2, N; X = C, N, but when X = N, R1 is absent; R1 = H, halo, alkyl, haloalkyl, alkoxy, cyano, CONR4R5, cycloalkyl; R2 = H, cyano, CONR4R5, CO2R4; R3 = H, cyano, CONR4R5, CO2R4, SO2R4; R4, R5 = H, alkyl, cycloalkyl were prepared as alpha 1a adrenergic receptor antagonists (no data). I may be used for treating benign prostatic hyperplasia (no data). E.g., reaction of (ClCH2CH2)2N(BOC) and 2-ClC6H4CH2CN in THF/DMF/NaH, followed by treatment of the piperidine product with HCl/HOAc gave 4-(2-chlorophenyl)-4-cyanopiperidine hydrochloride.

IT 135036-22-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperazine and piperidine derivs. as alpha 1a adrenergic receptor antagonists)

RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



IT 191156-64-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine and piperidine derivs. as alpha 1a adrenergic receptor antagonists)

RN 191156-64-6 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

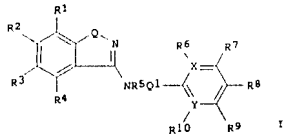
● HCl

L9 ANSWER 44 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:119141 CAPLUS
DOCUMENT NUMBER: 126:131469
TITLE: Preparation of 1-[N-(aralkylaminoalkyl)]aminoisoindoles as dopamine receptor ligands.
INVENTOR(S): He, Xiao-Shu; Decosta, Brian; Wasley, Jan W. F.
PATENT ASSIGNEE(S): Neurogen Corporation, USA; He, Xiao-Shu; Decosta, Brian; Wasley, Jan W. F.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9639403		A1	19961212	WO 1996-US8836	19960604 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI					
US 5602158		A	19970211	US 1995-464336	19950605 <--
US 5656632		A	19970812	US 1995-463037	19950605 <--
US 5744472		A	19980428	US 1995-463430	19950605 <--
AU 9659826		A	19961224	AU 1996-59826	19960604 <--
WO 9829410		A1	19980709	WO 1997-US967	19970102 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9715820		A	19980731	AU 1997-15820	19970102 <--
PRIORITY APPLN. INFO.:				US 1995-463037	A2 19950605
				US 1995-463430	A2 19950605
				US 1995-464336	A 19950710
				WO 1996-US8836	W 19960604
				WO 1997-US967	W 19970102

OTHER SOURCE(S): MARPAT 126:131469
GI

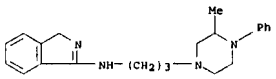


AB Title compds. (I; R1, R2, R3, R4, R7, R8, R9 = H, halo, OH, alkyl, alkoxy; X, Y, Z = C, N; R7R8 = atoms to form a (substituted) benzo ring; R6, R10 = H, halo, OH, alkyl, alkoxy, electron pair; R11 = R6, (substituted) Ph; R5 = H, alkyl; Q = (CH2)l; l = 1-4; Q1 = (CH2)mNR12CR14R15CR16R17ZR11R13(CH2)n; m = 2-5; n = 0-4; R12, R13 = alkyl; R12R13 = (CH2)s; s = 1-6; R14-R17 = H, alkyl, were prepared Thus, phthalimidine was stirred with Me3OBF4 to give a residue which was refluxed with 1-(3-aminopropyl)-4-(2-pyrimidinyl)piperazine and Et3N in CHCl3 to give 1-[3-[1-[4-(2-pyrimidinyl)piperazinyl]propyl]amino]isoindole. The latter bound to D4 receptors with Ki = 0.070 mM.

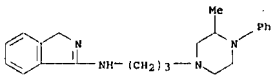
IT 186345-23-3P 186345-30-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-[N-(aralkylaminoalkyl)]aminoisoindoles as dopamine

receptor ligands)

RN 186345-23-3 CAPLUS
CN 1H-Isoindol-3-amine, N-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



RN 186345-30-2 CAPLUS
CN 1H-Isoindol-3-amine, N-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]-, dihydrobromide (9CI) (CA INDEX NAME)



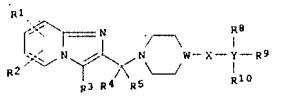
●2 HBr

L9 ANSWER 45 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:628533 CAPLUS
DOCUMENT NUMBER: 125:275875
TITLE: Preparation of imidazo[1,2-a]pyridines dopamine D4-receptor antagonist cardiovascular and CNS agents
INVENTOR(S): Tenbrink, Ruth E.
PATENT ASSIGNEE(S): Pharmacia and Upjohn Company, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9625414	A1	19960822	WO 1996-US1114	19960212 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD				
AU 9648595	A	19960904	AU 1996-48595	19960212 <--
EP 809642	A1	19971203	EP 1996-904507	19960212 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV					
JP 11500123	T	19990106	JP 1996-524966	19960212 <--
US 5912246	A	19990615	US 1997-894179	19970814 <--
US 6013654	A	20000111	US 1998-222560	19981230 <--
PRIORITY APPLN. INFO.:			US 1995-388682	A2 19950215
			WO 1996-US1114	W 19960212
			US 1997-894179	A3 19970814

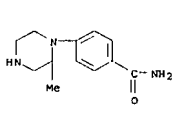
OTHER SOURCE(S): MARPAT 125:275875
GI



AB The title compds. (I; R1, R2 = H, halogen, alkyl, cycloalkyl, CN, (un)substituted CONH2, etc.; R3 = H, halogen, CN, OH, alkyl, CHO, etc.; R4-R7 = H, alkyl, cycloalkyl, cycloalkyl, (un)substituted aryl, etc.; R8-R10 = H, halogen, alkyl, cycloalkyl, CN, (un)substituted CONH2, (un)substituted NH2, etc.; W = N, CH; X = direct bond, NR4; Y = Ph, 2-, 3-, 4-pyridyl, pyrimidinyl, pyrazinyl, etc.] [e.g., 6-chloro-2-[[4-(4-methoxyphenyl)-1-piperazinyl]methyl]imidazo[1,2-a]pyridine; m.p. 111-112°], which are dopamine D4-receptor antagonists (e.g., I demonstrate a ki for displacement of 3H-spiperone from human dopamine D4 receptors of <2.5 μM), useful as antipsychotic (no data) and cardiovascular (no data) agents, are prepared

IT 182181-44-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of imidazo[1,2-a]pyridines dopamine D4-receptor antagonist cardiovascular and CNS agents)

RN 182181-44-8 CAPLUS
CN Benzamide, 4-(2-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

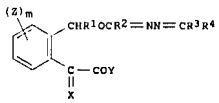


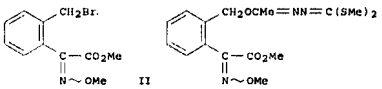
L9 ANSWER 46 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:494058 CAPLUS
DOCUMENT NUMBER: 125:142292
TITLE: Preparation of benzyloxyhydrazone derivatives as agrochemical fungicides
INVENTOR(S): Nishida, Tatsuki; Tajima, Sokichi; Tsubata, Kenji
PATENT ASSIGNEE(S): Nihon Nohyaku Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 56 pp.

CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08127563	A	19960521	JP 1994-288799	19941029 <--
PRIORITY APPLN. INFO.:			JP 1994-288799	19941029

OTHER SOURCE(S): MARPAT 125:142292
GI

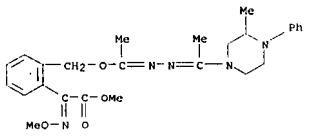




AB The title compds. [I; R1, R2 = H, C1-6 (halo)alkyl; R3, R4 = H, cyano, C1-6 (halo)alkyl, C3-6 cycloalkyl, etc.; X = CHOR5, NOR5 (wherein R5 = C1-6 alkyl); Y = C1-6 alkoxy, alkylthio, mono- or disubstituted amino; Z = halo, C1-6 (halo)alkyl; m = 0-4], effective agrochem. fungicides at low doses, are prepared Reaction of bromide II with AcNHN:C(SMe)2 in the presence of powdered KOH in DMSO at room temperature gave 42% hydrazone compound III, which showed 95-100% control of barley powdery mildew and Phytophthora infestans at 200 ppm.

IT 179935-74-1P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzyloxyhydrazone derivs. as agrochem. fungicides)

RN 179935-74-1 CAPLUS
CN Benzeneacetic acid, α-(methoxyimino)-2-[[1-[[3-methyl-4-phenyl-1-piperazinyl]ethylidene]hydrazono]ethoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)



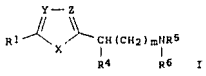
L9 ANSWER 47 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:467020 CAPLUS
DOCUMENT NUMBER: 125:114630
TITLE: Certain 4-aminomethyl-2-substituted imidazole derivatives and 2-aminomethyl-4-substituted imidazole derivatives; new classes of dopamine receptor subtype specific ligands
INVENTOR(S): Thurkauf, Andrew; Horvath, Raymond F.; Yuan, Jun; Peterson, John M.
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9616040	A1	19960530	WO 1995-US15262	19951122 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5681956	A	19971028	US 1995-401201	19950309 <--
US 5633377	A	19970527	US 1995-462833	19950605 <--
US 5646281	A	19970708	US 1995-461135	19950605 <--
US 5656762	A	19970812	US 1995-461858	19950605 <--
US 5712392	A	19980127	US 1995-464548	19950605 <--
AU 9643689	A	19960617	AU 1996-43689	19951122 <--
ZA 9509910	A	19970822	ZA 1995-9910	19951122 <--
ZA 9509911	A	19970822	ZA 1995-9911	19951122 <--
EP 793653	A1	19970910	EP 1995-942473	19951122 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
ZA 9707500	A	19980223	ZA 1997-7500	19951122 <--
JP 10502670	T	19980310	JP 1995-517074	19951122 <--
JP 2941950	B2	19990830		
BR 9509760	A	19980630	BR 1995-9760	19951122 <--
US 6069251	A	20000530	US 1997-859861	19970521 <--
US 6358955	B1	20020319	US 2000-497988	20000204 <--
US 2002143044	A1	20021003	US 2002-100691	20020318 <--
US 6797824	B2	20040928		

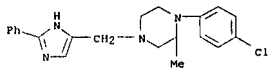
PRIORITY APPLN. INFO.: US 1994-344154 A2 19941123

US 1994-344552	A2	19941123
US 1995-401201	A2	19950309
US 1990-635256	A2	19901228
US 1993-61317	A2	19931108
US 1994-313435	A2	19940927
US 1995-462833	A1	19950605
WO 1995-US15262	W	19951122
US 1997-859861	A1	19970521
US 2000-497988	A1	20000204

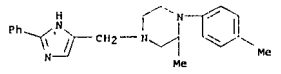
OTHER SOURCE(S): MARPAT 125:114630
GI



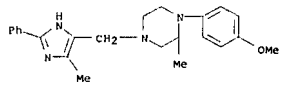
AB Disclosed are compds. (I), wherein R1 represents optionally substituted aryl, heteroaryl, arylalkyl, or cycloalkyl groups; X, Z, and Y are optionally substituted nitrogen or carbon atoms; R3 and R4 are organic or inorg. substituents which may together form ring structures; m is zero, one or two; and R5 and R6 are organic or inorg. substituents; and the pharmaceutically acceptable addition salts thereof, which compds. are highly selective partial agonists or antagonists at brain dopamine receptor subtypes or prodrugs thereof and are useful in the diagnosis and treatment of affective disorders such as schizophrenia and depression as well as certain movement disorders such as Parkinsonism. Specifically, 2-phenyl-4(S)-[(4-(2-pyrimidinyl)piperazin-1-yl)methyl]imidazole dihydrochloride was prepared and was shown to bind to the dopamine D4 receptor site (Ki = 1033, 8200, 2.7 for D2, D3, D4 binding sites, resp.).
IT 179333-05-2P 179333-06-3P 179333-36-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazole derivs. as dopamine receptor partial agonists or antagonists for memory enhancement and treatment of schizophrenia and depression and Parkinsonism)
RN 179333-05-2 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-4-[(2-phenyl-1H-imidazol-4-yl)methyl]- (9CI) (CA INDEX NAME)



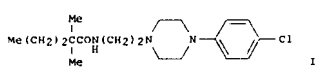
RN 179333-06-3 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)-4-[(2-phenyl-1H-imidazol-4-yl)methyl]- (9CI) (CA INDEX NAME)



RN 179333-36-9 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl-4-[(5-methyl-2-phenyl-1H-imidazol-4-yl)methyl]- (9CI) (CA INDEX NAME)

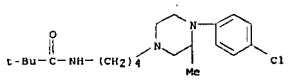


L9 ANSWER 48 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:368754 CAPLUS
DOCUMENT NUMBER: 125:104240
TITLE: N-(substituted-phenyl)piperazines: antagonists with high binding and functional selectivity for dopamine D4 receptors
AUTHOR(S): Boyfield, Izzy; Coldwell, Martyn C.; Hadley, Michael S.; Healy, Maureen A. M.; Johns, Amanda; Nash, David J.; Riley, Graham J.; Scott, Emma E.; Smith, Stephen A.; et al.
CORPORATE SOURCE: SmithKline Beecham Pharm., Harlow, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(11), 1227-1232
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB A series of N-(substituted-phenyl)piperazine derivs. was prepared as selective antagonists of the dopamine D4 receptor. Many analogs possessed a binding selectivity of over 100 fold for D4 over D2 receptors. In functional studies in the microphysiometer, compound I showed a selectivity over dopamine D2 receptors of greater than 1000 fold.
IT 179258-15-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-(substituted-phenyl)piperazines as D4 receptor antagonists in relation to schizophrenia)

RN 179258-15-2 CAPLUS
CN Propanamide, N-[4-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]butyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)

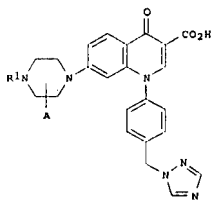


L9 ANSWER 49 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:225867 CAPLUS
DOCUMENT NUMBER: 124:261076
TITLE: Preparation of 7-piperazinyl-1,4-dihydro-4-oxo-1-[4-(1H-1,2,4-triazol-1-yl-methyl)phenyl]quinoline-3-carboxylic acids as virucides.
INVENTOR(S): Bender, Wolfgang; Roeben, Wolfgang; Paesens, Arnold; Bartel, Stephan
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 40 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4425660	A1	19960125	DE 1994-4425660	19940720 <--
WO 9602532	A1	19960201	WO 1995-EP2643	19950707 <--
W: AU, CA, CN, CZ, FI, HU, JP, KR, LT, MX, NO, NZ, PL, RU, SI, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9530763	A	19960216	AU 1995-30763	19950707 <--
ZA 9506012	A	19960222	ZA 1995-6012	19950719 <--

PRIORITY APPLN. INFO.: DE 1994-4425660 A 19940720
WO 1995-EP2643 W 19950707

OTHER SOURCE(S): CASREACT 124:261076; MARPAT 124:261076
GI



AB Title compds. [I; A = H, Me; R1 = (substituted) Ph, naphthyl, pyridyl, pyrimidinyl, pyrazinyl, 3,4-methylenedioxyphenyl], were prepared Thus, 7-fluoro-1,4-dihydro-4-oxo-1-[4-(1H-1,2,4-triazol-1-ylmethyl)phenyl]-3-quinolinecarboxylic acid hydrochloride [preparation via 1-(4-aminobenzyl)-1H-1,2,4-triazole given] was stirred with 1-(o-fluorophenyl)piperazine and diisopropylamine in DMF at 120° to give 95.4% I (A = H; R1 = o-fluorophenyl). I inhibited HIV in human lymphocytes with IC50 = 0.08-0.7 μM.

IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 7-piperazinyl-1,4-dihydro-4-oxo-1-[4-(1H-1,2,4-triazol-1-ylmethyl)phenyl]quinoline-3-carboxylic acids as virucides)

RN 2946-76-1 CAPLUS

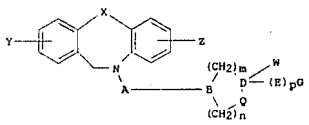
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 50 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:958518 CAPLUS
DOCUMENT NUMBER: 124:146212
TITLE: 8-Chloro-10,11-dihydro-10-(1-piperazinylcarbonyl)dibenz[b,f][1,4]oxazepine derivatives and analogs as analgesics and prostaglandin-E2 antagonists
INVENTOR(S): Hansen, Donald W., Jr.; Peterson, Karen B.
PATENT ASSIGNEE(S): G. D. Searle and Co., USA
SOURCE: U.S., 38 pp. Cont.-in-part of U.S. 5,354,747.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

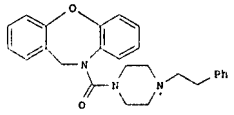
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5461047	A	19951024	US 1994-245349	19940518 <--
US 5354747	A	19941011	US 1993-79021	19930616 <--
CA 2165159	A1	19941222	CA 1994-2165159	19940602 <--
WO 9429286	A1	19941222	WO 1994-US6029	19940602 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9471387	A	19950103	AU 1994-71387	19940602 <--
EP 703908	A1	19960403	EP 1994-920687	19940602 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09500107	T	19970107	JP 1994-501874	19940602 <--
PRIORITY APPLN. INFO.:			US 1993-79021	A2 19930616
			US 1994-245349	A 19940518
			WO 1994-US6029	W 19940602

OTHER SOURCE(S): CASREACT 124:146212; MARPAT 124:146212

GI



I



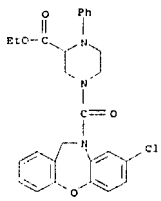
II

AB The present invention provides substituted dibenzoxazepine and dibenzothiazepine compds. I or a pharmaceutically-acceptable salt thereof, wherein: W = (H)r; Q = (CH(R)q)t; X is oxygen, sulfur, SO, or SO2; Y is hydrogen, halogen or hydroxy; Z is hydrogen or halogen; A is alkylene or carbonyl; B is CH or nitrogen; D is carbon or nitrogen; E is alkylene, carbonyl, alkyleneamino or alkylenecarbonyl; G is hydrogen, alkyl, cycloalkyl, alkoxy, aminoalkyl, aminocycloalkyl, aryl, alkylenearyl or aryl-substituted aryl; R is hydrogen or CO2R1 ; R1 is hydrogen or alkyl; m is an integer of from 0 to 4; n is an integer of from 0 to 4; r is 0 or 1; q is an integer of from 0 to 1; t is an integer of from 0 to 1; and p is an integer of from 0 to 1 (with provisos) which are useful as analgesic agents for the treatment of pain, and for prostaglandin-E2 mediated diseases. Thus, e.g., 10,11-dihydro-10-[[4-(2-phenylethyl)-1-piperazinyl]carbonyl]dibenz[b,f][1,4]oxazepine, monohydrochloride (II.HCl) was synthesized by reductive alkylation of 8-chloro-10,11-dihydro-10-(1-piperazinylcarbonyl)dibenz[b,f][1,4]oxazepine, monohydrochloride (preparation given) with phenylacetaldehyde, and exhibited analgesic activity of 10/10 in the writhing assay and prostaglandin-E2 antagonism with dose ratio of EC50 dose = 2.6.

IT 163839-09-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(8-chloro-10,11-dihydro-10-(1-piperazinylcarbonyl)dibenz[b,f][1,4]oxazepine derivs. and analogs as analgesics and prostaglandin-E2 antagonists)

RN 163839-09-6 CAPLUS

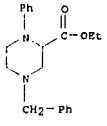
CN 2-Piperazinecarboxylic acid, 4-[(8-chlorodibenz[b,f][1,4]oxazepin-10(11H)-yl)carbonyl]-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



IT 162082-37-3P, Ethyl 1-phenyl-4-(phenylmethyl)-2-piperazinecarboxylate 162082-38-4P, Ethyl 1-phenyl-2-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(8-chloro-10,11-dihydro-10-(1-piperazinylcarbonyl)dibenz[b,f][1,4]oxazepine derivs. and analogs as analgesics and prostaglandin-E2 antagonists)

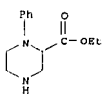
RN 162082-37-3 CAPLUS

CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 162082-38-4 CAPLUS

CN 2-Piperazinecarboxylic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



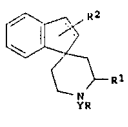
L9 ANSWER 51 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:954796 CAPLUS

DOCUMENT NUMBER: 123:330860
TITLE: Tocolytic oxytocin receptor antagonists
INVENTOR(S): Bock, Mark G.; Evans, Ben E.; Culberson, J. Christopher; Gilbert, Kevin F.; Rittle, Kenneth E.; Williams, Peter D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

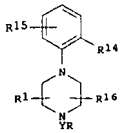
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9525443	A1	19950928	WO 1995-US3738	19950323 <--
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5464788	A	19951107	US 1994-217270	19940324 <--
CA 2186129	A1	19950928	CA 1995-2186129	19950323 <--
AU 9521952	A	19951009	AU 1995-21952	19950323 <--
AU 686792	B2	19980212		
EP 751773	A1	19970108	EP 1995-914875	19950323 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09512521	T	19971216	JP 1995-524838	19950323 <--
US 5756504	A	19980526	US 1996-718415	19960923 <--
PRIORITY APPLN. INFO.:			US 1994-217270	A2 19940324
			WO 1995-US3738	W 19950323

OTHER SOURCE(S): MARPAT 123:330860

GI



I



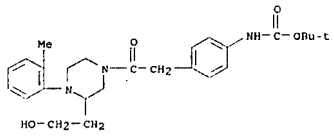
II

AB Spiroindenepiperidine derivs. I [R1 = H, C1-5 alkyl, CN, CO2H, Ph, etc.; R2 = H, PhCH2, C3-8 cycloalkyl, C1-5 alkyl; Y = CO, C(O)NR2, C(:NR2), SO2, C(O)(CH2)n, (CH2)p, (CH2)pC(O); R = (tetrahydro)naphthyl, (substituted) cyclohexyl, (substituted) Ph, heterocyclyl; bond in cyclopentane ring is single or double; n = 0-3; p = 1-3] and phenylpiperazine derivs. II (Y, R, R1 as above; R14, R15 = H, C1-5 alkyl, C1-5 alkoxy, halo, NO2, CN; R16 = H, :O) and their pharmaceutically acceptable salts and esters are useful as oxytocin and vasopressin receptor antagonists for treatment of preterm labor and dysmenorrhea and for stopping labor prior to cesarean delivery. Thus, 1-[2-methoxy-4-[1-[2-

(N-cyclopropylamino)ethylsulfonyl]-4-piperidyloxy]phenylacetyl]-4-(2-methylphenyl)piperazine-2-carboxamide (III) was prepared in 11 steps from 4-hydroxypiperidine, Me 2,4-dihydroxybenzoate, 2-benzylaminoethanol, o-toluidine, 2,3-dibromopropionamide, and cyclopropylamine. III competed with 1 nM oxytocin-3H for binding to rat uterine tissue with an IC50 of 20 nM.

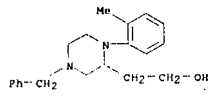
IT 170929-79-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tocolytic oxytocin receptor antagonists)

RN 170929-79-0 CAPLUS
CN Carbamic acid, [4-[2-[3-(2-hydroxyethyl)-4-(2-methylphenyl)-1-piperazinyl]-2-oxoethyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

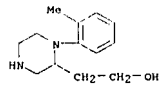


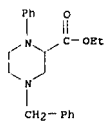
IT 170930-08-2P 170930-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tocolytic oxytocin receptor antagonists)

RN 170930-08-2 CAPLUS
CN 2-Piperazineethanol, 1-(2-methylphenyl)-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

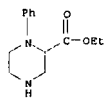


RN 170930-09-3 CAPLUS
CN 2-Piperazineethanol, 1-(2-methylphenyl)- (9CI) (CA INDEX NAME)



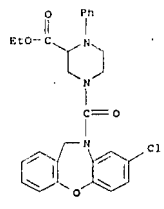


RN 162082-38-4 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



IT 163839-09-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dibenz[b,f][1,4]oxazepines analgesics)

RN 163839-09-6 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-[(8-chlorodibenz[b,f][1,4]oxazepin-10(11H)-yl)carbonyl]-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

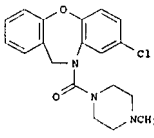


L9 ANSWER 53 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:274966 CAPLUS
DOCUMENT NUMBER: 122:81403
TITLE: Preparation of 3-(piperazinomethyl)indazoles as dopaminergic antagonists
INVENTOR(S): Baker, Raymond; Kulagowski, Janusz Jozef; Leeson, Paul David; Smith, Adrian Leonard

L9 ANSWER 52 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:682580 CAPLUS
DOCUMENT NUMBER: 123:83397
TITLE: Analgesic dibenzoxazepines and dibenzothiazepines
INVENTOR(S): Hansen, Donald Willis, Jr.; Peterson, Karen Berenice
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9429286	A1	19941222	WO 1994-US6029	19940602 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5354747	A	19941011	US 1993-79021	19930616 <--
US 5461047	A	19951024	US 1994-245349	19940518 <--
AU 9471387	A	19950103	AU 1994-71387	19940602 <--
EP 703908	A1	19960403	EP 1994-920687	19940602 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09500107	T	19970107	JP 1994-501874	19940602 <--
PRIORITY APPLN. INFO.:			US 1993-79021 A	19930616
			US 1994-245349 A	19940518
			WO 1994-US6029 W	19940602

OTHER SOURCE(S): MARPAT 123:83397
GI



I

AB Dibenz[b,f][1,4]oxazepines and dibenz[b,f][1,4]thizepines were disclosed for the treatment of prostaglandin-E2 mediated diseases. A claimed example compound is 8-chloro-10,11-dihydro-10-[[4-(phenylmethyl)-1-piperazinyl]carbonyl]dibenz[b,f][1,4]oxazepine hydrochloride (I).

IT 162082-37-3P 162082-38-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dibenz[b,f][1,4]oxazepines analgesics)

RN 162082-37-3 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)

PATENT ASSIGNEE(S): Merck Sharp and Dohme Ltd., UK
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421630	A1	19940929	WO 1994-GB504	19940314 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2156838	A1	19940929	CA 1994-2156838	19940314 <--
AU 9462140	A	19941011	AU 1994-62140	19940314 <--
AU 685090	B2	19980115		
EP 689539	A1	19960103	EP 1994-909210	19940314 <--
EP 689539	B1	19971203		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08512284	T	19961224	JP 1994-520766	19940314 <--
AT 160779	T	19971215	AT 1994-909210	19940314 <--
ES 2110225	T3	19980201	ES 1994-909210	19940314 <--
US 5780475	A	19980714	US 1995-525629	19951229 <--
PRIORITY APPLN. INFO.:			GB 1993-5623 A	19930318
			WO 1994-GB504 W	19940314

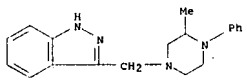
OTHER SOURCE(S): MARPAT 122:81403
GI

I

AB Title compds. [I; R = H, alkyl; R1 = H, (cyclo)alkyl, alkoxy, (hetero)aryl, etc.; R2 = (cyclo)alkyl, alkoxy, (hetero)aryl, etc.; R3-R5 = H, halo, cyano, hydrocarbyl, etc.] were prepared Thus, 1H-indazole-3-carboxylic acid was amidated by 1-(4-chlorophenyl)piperazine and the product reduced to give I (R = R1 = R3-R5 = H, R2 = 4-ClC6H4). I had Ki of 1.5μM for displacement of spiperone from cloned human dopamine D4 receptors in vitro.

IT 160008-87-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-(piperazinomethyl)indazoles as dopaminergic antagonists)

RN 160008-87-7 CAPLUS
CN 1H-Indazole, 3-[(3-methyl-4-phenyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

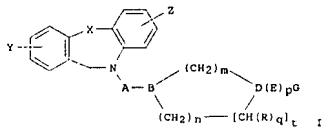


L9 ANSWER 54 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:205963 CAPLUS
DOCUMENT NUMBER: 123:9468
TITLE: 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9- and/or 10-substituted dibenzoxazepine and dibenzthiazepine compounds as analgesics and prostaglandin E2 antagonists, pharmaceutical compositions and methods of use
INVENTOR(S): Hansen, Donald W., Jr.; Peterson, Karen B.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 39 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

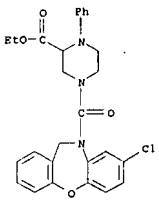
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5354747	A	19941011	US 1993-79021	19930616 <--
US 5461047	A	19951024	US 1994-245349	19940518 <--
CA 2165159	A1	19941222	CA 1994-2165159	19940602 <--
WO 9429286	A1	19941222	WO 1994-US6029	19940602 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9471387	A	19950103	AU 1994-71387	19940602 <--
EP 703908	A1	19960403	EP 1994-920687	19940602 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09500107	T	19970107	JP 1994-501874	19940602 <--

PRIORITY APPLN. INFO.: US 1993-79021 A2 19930616
US 1994-245349 A 19940518
WO 1994-US6029 W 19940602

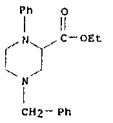
OTHER SOURCE(S): CASREACT 123:9468; MARPAT 123:9468
GI



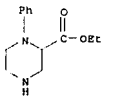
AB The present invention provides substituted dibenzoxazepine and dibenzthiazepine compds. I which are useful as analgesic agents for the treatment of pain, and for prostaglandin-E2 mediated diseases, pharmaceutical compns. comprising a therapeutically-effective amount of I in combination with a pharmaceutically-acceptable carrier, a method for eliminating or ameliorating pain in an animal comprising administering a therapeutically-effective amount of I to the animal, and a method for treating prostaglandin-E2 mediated diseases in an animal comprising administering a therapeutically-effective amount of I to the animal. Analgesic activity was measured using the writhing assay at standard dose of 10 mpk/g body weight: I produced analgesia in from 2/10 to 10/10 of the mice. Prostaglandin E2 antagonism assay (inhibition of contraction of guinea pig ileum): dose ratio of EC50 doses of from 0.8 to 32. Pharmaceutical compns. were given.
IT 163839-09-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(substituted dibenzoxazepine and dibenzthiazepine compds. as analgesics and prostaglandin E2 antagonists)
RN 163839-09-6 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-[(8-chlorodibenz[b,f][1,4]oxazepin-10(11H)-yl)carbonyl]-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



IT 162082-37-3P, Ethyl 1-Phenyl-4-(phenylmethyl)-2-piperazinecarboxylate 162082-38-4P, Ethyl 1-phenyl-2-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(substituted dibenzoxazepine and dibenzthiazepine compds. as analgesics and prostaglandin E2 antagonists)
RN 162082-37-3 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 162082-38-4 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

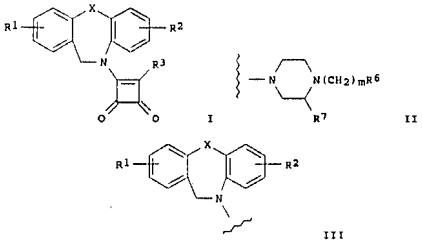


L9 ANSWER 55 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:205962 CAPLUS
DOCUMENT NUMBER: 122:239729
TITLE: Squaric acid derivatives of substituted dibenzoxazepine compounds as analgesics and prostaglandin E2 antagonists, pharmaceutical compositions and methods of use
INVENTOR(S): Chandrakumar, Nizal S.; Pitzele, Barnett S.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

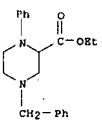
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5354746	A	19941011	US 1993-69503	19930601 <--
WO 9427981	A1	19941208	WO 1994-US4973	19940511 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9467831	A	19941220	AU 1994-67831	19940511 <--

PRIORITY APPLN. INFO.: US 1993-69503 A 19930601
WO 1994-US4973 W 19940511

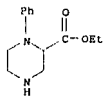
OTHER SOURCE(S): MARPAT 122:239729
GI



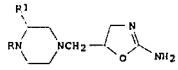
AB The present invention provides substituted dibenzoxazepine compds. of formula I (X = O, S, SO, SO2; R1, R2 = H, halogen; R3 = NR4R5, alkoxy, II, III; R4 = H, alkyl; R5 = alkyl, alkylene-NR4R4, alkylaryl; R6 = Me, aryl; R7 = H, CO2R4; m = 0-5) which are useful as analgesic agents for the treatment of pain, and as prostaglandin-E2 antagonists for the treatment of prostaglandin-E2 mediated diseases, pharmaceutical compns. comprising a therapeutically-effective amount of a compound I in combination with a pharmaceutically-acceptable carrier, a method for eliminating or ameliorating pain in an animal, and a method for treating prostaglandin-E2 mediated diseases in an animal, comprising administering a therapeutically-effective amount of a compound I Formula I to the animal. Analgesic activity assessed by writhing assay at 30 mg/kg dose: in from 4/10 to 6/10 of mice, the number of writhes elicited by PBQ was equal to, or less than, one-half the median number of writhes recorded for the saline-treated control group. PGE2 antagonism assay: EC50 dose ratios of 1.9 ± 0.9 to 153 ± 74 for inhibition of contraction of guinea pig ileum. Pharmaceutical formulations were given.
IT 162082-37-3P, Ethyl 1-phenyl-4-(phenylmethyl)-2-piperazinecarboxylate 162082-38-4P, Ethyl 1-phenyl-2-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(squaric acid derivs. of substituted dibenzoxazepine compds. as analgesics and prostaglandin E2 antagonists)
RN 162082-37-3 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)



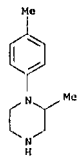
RN 162082-38-4 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



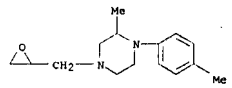
L9 ANSWER 56 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:457460 CAPLUS
DOCUMENT NUMBER: 121:57460
TITLE: 2-Amino-2-oxazolines. VII. Influence of structural parameters on the antidepressant activity of 5-(1-aryl-4-piperazino)methyl-2-amino-2-oxazolines
AUTHOR(S): Bosc, Jean Jacques; Forfar, Isabelle; Jarry, Christian; Laguerre, Michel; Carpy, Alain
CORPORATE SOURCE: Lab. Chim. Phys., Univ. Bordeaux II, Bordeaux, 33076, Fr.
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1994), 327(3), 187-92
CODEN: ARPMAS; ISSN: 0365-6233
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:57460
GI



AB [(Arylpiperazino)methyl]aminooxazolines I (R = substituted Ph, R1 = H, Me) were prepared and screened for antidepressant activity. Their lipophilic behavior is discussed in relation to the nature and the position of substituents on the aromatic ring. The influence of steric effects on the pharmacol. activity has been investigated using exptl. methods (x-ray diffraction, NMR) and theor. calcns. (semi-empirical quantum mechanics). Ortho-substitution on the Ph ring or C(α)-substitution on the piperazine ring by a Me group results in the same effects, i.e., an increase of the angle between the two rings up to 64° (x-ray and calcn.) and a loss of antidepressant activity.
IT 35947-11-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of epichlorohydrin)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)

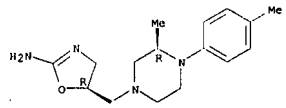


IT 155850-87-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cleavage of, with monosodium cyanamide)
RN 155850-87-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)-4-(oxiranylmethyl)- (9CI) (CA INDEX NAME)



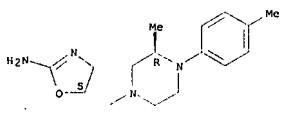
IT 155850-82-1P 155850-86-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, antidepressant activity, and NMR of)
RN 155850-82-1 CAPLUS
CN 2-Oxazolamine, 4,5-dihydro-5-[[3-methyl-4-(4-methylphenyl)-1-piperazinyl]methyl]-, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 155850-86-5 CAPLUS
CN 2-Oxazolamine, 4,5-dihydro-5-[[3-methyl-4-(4-methylphenyl)-1-piperazinyl]methyl]-, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

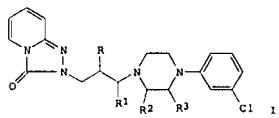


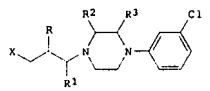
L9 ANSWER 57 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:8618 CAPLUS
DOCUMENT NUMBER: 120:8618
TITLE: Alkyl derivatives of trazodone with CNS activity and reduced side effects
INVENTOR(S): Baiocchi, Leandro
PATENT ASSIGNEE(S): Istituto Ricerca Francesco Angelini S.p.A., Italy
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9314091	A1	19930722	WO 1993-EP80	19930114 <--
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9333504	A	19930803	AU 1993-33504	19930114 <--
AU 671973	B2	19960919		
EP 623131	A1	19941109	EP 1993-902204	19930114 <--
EP 623131	B1	19960403		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07503000	T	19950330	JP 1993-512150	19930114 <--
JP 2856912	B2	19990210		
HU 70761	A2	19951030	HU 1994-2119	19930114 <--
HU 218678	B	20001028		
AT 136307	T	19960415	AT 1993-902204	19930114 <--
HU 72591	A2	19960528	HU 1995-2179	19930114 <--
HU 217968	B	20000528		
ES 2088270	T3	19960801	ES 1993-902204	19930114 <--
BR 9305752	A	19970128	BR 1993-5752	19930114 <--
PL 170913	B1	19970228	PL 1993-304665	19930114 <--
CZ 282910	B6	19971112	CZ 1994-1732	19930114 <--
RO 113465	B1	19980730	RO 1994-1203	19930114 <--
RU 2126801	C1	19990227	RU 1994-36769	19930114 <--
SK 280561	B6	20000313	SK 1994-846	19930114 <--
CA 2128202	C	20010123	CA 1993-2128202	19930114 <--
ZA 9300292	A	19930819	ZA 1993-292	19930115 <--
FI 9403386	A	19940715	FI 1994-3386	19940715 <--
FI 110186	B1	20021213		
NO 9402668	A	19940916	NO 1994-2668	19940715 <--
NO 302365	B1	19980223		
US 5543563	A	19960806	US 1995-457490	19950601 <--
US 5739334	A	19980414	US 1995-457114	19950601 <--
HU 71511	A2	19951228	HU 1995-2177	19950719 <--
HU 219493	B	20010428		

HU 71512	A2	19951228	HU 1995-2178	19950719 <--
HU 217981	B	20000528		
HU 71513	A2	19951228	HU 1995-2180	19950719 <--
HU 217982	B	20000528		
US 5726178	A	19980310	US 1996-758556	19961129 <--
NO 9704462	A	19940916	NO 1997-4462	19970926 <--
FI 2002001652	A	20020916	FI 2002-1652	20020916 <--
FI 113266	B1	20040331		
PRIORITY APPLN. INFO.:			IT 1992-MI84	A 19920117
			HU 1994-2119	A 19930114
			WO 1993-EP80	A 19930114
			US 1994-256352	A3 19940718

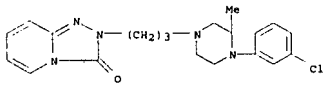
OTHER SOURCE(S): MARPAT 120:8618
GI



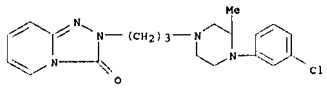


II

AB The title compds. I (only one of R, R1-R3 is C1-3 alkyl and the others are H), useful in the treatment of depression, and which have reduced affinity for adrenergic receptors thus not producing the side effects of trazodone (e.g., hypotension and priapism), are prepared by reacting 1,2,4-triazolo[4,3-a]pyridon-3-(2H)-one or its salts with alkali metal and with piperazine derivative II (X = leaving group). Thus, the Na salt of 1,2,4-triazolo[4,3-a]pyridin-3-2H)-one was condensed with 1-(3-chlorophenyl)-4-(3-chloro-2-methylpropyl)piperazine, producing I (R = Me, R1-R3 = H) hydrochloride salt, m.p. 196-198°, which demonstrated 27% inhibition of adrenergic α1-receptors at 10-7 M and 88% inhibition at 10-5 M, vs. 49% and 98%, resp., for trazodone.
IT 151448-01-0P 151448-02-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antidepressant with reduced adrenergic receptor affinity and side effects)
RN 151448-01-0 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



RN 151448-02-1 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



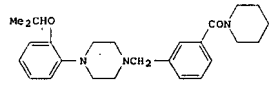
● HCl

L9 ANSWER 58 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:517276 CAPLUS
DOCUMENT NUMBER: 119:117276
TITLE: Novel 4-arylpiperazines and 4-arylpiperidines
INVENTOR(S): Reitz, Allen B.
PATENT ASSIGNEE(S): McNeilab, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9304682	A1	19930318	WO 1992-US7754	19920911	<--
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MW, NO, RO, RU, SD					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG					
ZA 9109629	A	19931206	ZA 1991-9629	19911205	<--
HU 68963	A2	19950828	HU 1993-1362	19911220	<--
HU 217068	B	19991129			
AU 9226599	A	19930405	AU 1992-26599	19920911	<--
AU 657799	B2	19950323			
EP 563345	A1	19931006	EP 1992-920313	19920911	<--
EP 563345	B1	20020703			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE					
HU 64535	A2	19940128	HU 1993-1361	19920911	<--
JP 06502870	T	19940331	JP 1993-505525	19920911	<--
JP 2941945	B2	19990830			
RU 2139867	C1	19991020	RU 1993-41055	19920911	<--
SG 70980	A1	20000321	SG 1996-5506	19920911	<--
AT 219938	T	20020715	AT 1992-920313	19920911	<--

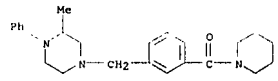
ES 2179822	T3	20030201	ES 1992-920313	19920911	
NO 9301695	A	19930527	NO 1993-1695	19930510	<--
NO 9301694	A	19930630	NO 1993-1694	19930510	<--
NO 303780	B1	19980831			
FI 111639	B1	20030829	FI 1993-2104	19930510	
US 5569659	A	19961029	US 1995-442600	19950517	<--
PRIORITY APPLN. INFO.:			US 1991-757881	A 19910911	
			US 1992-944006	B1 19920911	
			WO 1992-US7754	A 19920911	
			WO 1992-US9082	W 19921220	
			US 1994-365978	B1 19941228	

OTHER SOURCE(S): MARPAT 119:117276
GI

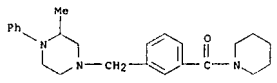


I

AB Title compds.4-RX(CH2)nCR1R2X1WNR3R4 [X = (un)substituted piperazino, piperidino; X1 = (un)substituted Ph; R = aryl; CR1R2 = CH2, CO, 1,1-alkanediyl, CHOH; W = CO, CS, SO2; NR3R4 = amino; n = 0-4] (113 compds.) were prepared as antipsychotic agents. Thus, 3-ClCH2C6H4COCl was treated with piperidine and N-(2-isopropoxyphenyl)piperazine to give the piperazine I which had an ED50 against apomorphine-induced emesis in dogs of 0.038mg/kg orally in dogs 1h before treatment with apomorphine..
IT 148826-90-8P 148853-59-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antipsychotic activity of)
RN 148826-90-8 CAPLUS
CN Piperidine, 1-[3-[(3-methyl-4-phenyl-1-piperazinyl)methyl]benzoyl]- (9CI) (CA INDEX NAME)



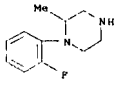
RN 148853-59-2 CAPLUS
CN Piperidine, 1-[3-[(3-methyl-4-phenyl-1-piperazinyl)methyl]benzoyl]-, monohydrochloride (9CI) (CA INDEX NAME)



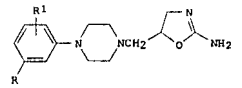
● HCl

IT 2946-76-1 148888-23-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation from, of antipsychotic arylpiperidines and arylpiperazines)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

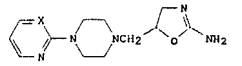
RN 148888-23-7 CAPLUS
CN Piperazine, 1-(2-fluorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 59 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:182780 CAPLUS
DOCUMENT NUMBER: 118:182780
TITLE: RP-HPLC of new antidepressant 2-amino-2-oxazolines: a comparative study of their lipophilicity
AUTHOR(S): Desmotes-Mainard, F.; Thomas, J.; Bosc, J. J.; Devaux, G.; Jarry, C.
CORPORATE SOURCE: Dep. Pharmacol. Clin., CHR Pellegrin, Fr.
SOURCE: Journal of Liquid Chromatography (1993), 16(3), 767-76
CODEN: JLCHD8; ISSN: 0148-3919
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

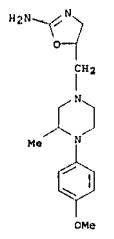


I



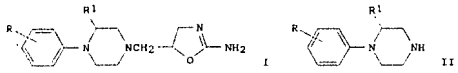
II

AB A comparative study of lipophilicity in a series of 5-(1-aryl-4-piperazino)methyl-2-amino-2-oxazolines, i.e., I (R = H, Me; R1 = H, Cl, F, Me, MeO, EtO, OH, CF3, Me2CH, NMe2, etc.) and II (X = CH, N), with antidepressant activity has been carried out using a RP-HPLC technique. This chromatog. method allowed the determination of log k'w values (k' = chromatog. column capacity factor) through extrapolation to 100% water from capacity factors data. The partition coeffs. (log Po/w) and ionization consts. (pKa) were measured by classical methods. A good correlation between log Po/w and log k'w was found, confirming the feasibility of using the latter as a lipophilicity descriptor. In this homogeneous chemical series the nature and the position of the substituents on the aromatic ring did not induce important variations on the pKa values, whereas they accounted for a great part in lipophilicity data.
IT 144881-48-1
RL: PRP (Properties)
(lipophilicity of, HPLC study of, structure in relation to)
RN 144881-48-1 CAPLUS
CN 2-Oxazolamine, 4,5-dihydro-5-[[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 60 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:38880 CAPLUS
DOCUMENT NUMBER: 118:38880

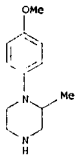
TITLE: Synthesis and antidepressant activity of 5-(1-aryl-4-piperazino)methyl-2-amino-2-oxazolines
AUTHOR(S): Bosc, J. J.; Jarry, C.; Carpy, A.; Panconi, E.; Descas, P.
CORPORATE SOURCE: Lab. Chim. Phys., Univ. Bordeaux II, Bordeaux, 33076, Fr.
SOURCE: European Journal of Medicinal Chemistry (1992), 27(5), 437-42
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The synthesis of 20 5-(1-aryl-4-piperazino)methyl-2-amino-2-oxazolines, e.g., I (R = H, 2-, 3-, 4-Cl, 3,4-Cl2, 3-, 4-Me, 4-MeO, 4-Me2N; R1 = H, Me), from arylpiperazines II and epichlorhydrin is described. I(R = H, 4-OMe, 4-OH, 4-OAc, R1 = H) had ED50 <20mg/kg orally in the reserpine-induced hypothermia test in mice. Structure-activity relationships were studied and correlated with the nature of the aromatic substituent. Preliminary lipophilic and electronic properties of I (R, R1 = H) are reported.

IT 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction of, with epichlohydrin in synthesis of arylpiperazinylmethylaminooxazoline)

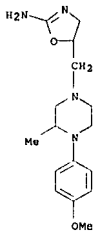
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



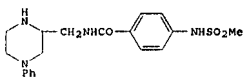
IT 144881-48-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antidepressant activity of)

RN 144881-48-1 CAPLUS
CN 2-Oxazolamine, 4,5-dihydro-5-[[4-(4-methoxyphenyl)-3-methyl-1-

piperazinyl]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 61 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:106235 CAPLUS
DOCUMENT NUMBER: 116:106235
TITLE: Synthesis, cardiac electrophysiology, and β-blocking activity of novel arylpiperazines with potential as class II/III antiarrhythmic agents
AUTHOR(S): Phillips, Gary B.; Morgan, Thomas K., Jr.; Lumma, William C., Jr.; Gomez, Robert P.; Lind, Joan M.; Lis, Randall; Argentieri, Thomas; Sullivan, Mark E.
CORPORATE SOURCE: Dep. Med. Chem., Berlex Lab., Inc., Cedar Knolls, NJ, 07927, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(4), 743-50
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:106235
GI

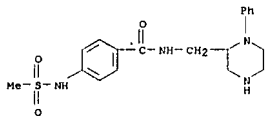


AB Cyclocondensation reaction of N-aryl-N'-(phenylmethyl)-1,2-ethanediamine with 2,3-dibromopropionamide followed by derivatization gave a series of novel arylpiperazines, e.g., I. Thus, the key step in the preparation of the new compds. involves a regioselective heterocyclic ring formation. These were prepared in an attempt to incorporate both class II (β-receptor blocking) and class III antiarrhythmic properties in a single mol. All but four compds. significantly prolonged action potential duration in

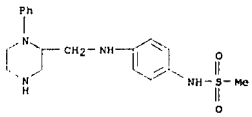
canine cardiac Purkinje fibers (class III activity). All but one of the compds. demonstrated β-receptor affinity in a competitive binding assay and three had β1-receptor selectivity. Compared to sotalol, a reference class II/III agent, I demonstrated β1-selectivity and was 1 order of magnitude more potent in the in vitro class III and the β1-receptor screens. I was evaluated further and found to be effective in preventing programmed elec. stimulation-induced arrhythmias in conscious dogs (class III activity) and against epinephrine-induced arrhythmias in halothane anesthetized dogs (class II activity).

IT 135036-09-8P 135036-10-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antiarrhythmic activity of)

RN 135036-09-8 CAPLUS
CN Benzamide, 4-[(methylsulfonyl)amino]-N-[(1-phenyl-2-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

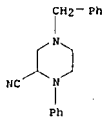


RN 135036-10-1 CAPLUS
CN Methanesulfonamide, N-[4-[[(1-phenyl-2-piperazinyl)methyl]amino]phenyl]- (9CI) (CA INDEX NAME)

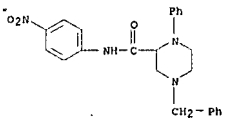


IT 135036-22-5P 135063-15-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



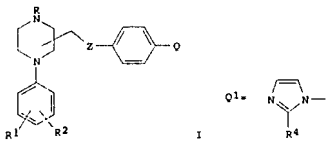
RN 135063-15-9 CAPLUS
CN 2-Piperazinecarboxamide, N-(4-nitrophenyl)-1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



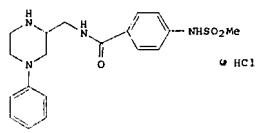
L9 ANSWER 62 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:471649 CAPLUS
DOCUMENT NUMBER: 115:71649
TITLE: Preparation of N-arylpiperazinylmethylamides as antiarrhythmics.
INVENTOR(S): Lumma, William Carl, Jr.; Morgan, Thomas Kenneth, Jr.; Phillips, Gary Bruce
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9104250	A1	19910404	WO 1990-EP1059	19900702	<--
W: CA, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE					
US 5051422	A	19910924	US 1989-408020	19890915	<--
CA 2067156	A1	19910316	CA 1990-2067156	19900702	<--
EP 491709	A1	19920701	EP 1990-911657	19900702	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE					
JP 05500660	T	19930212	JP 1990-510812	19900702	<--
US 5223623	A	19930629	US 1991-757741	19910911	<--
PRIORITY APPLN. INFO.:			US 1989-408020	A 19890915	
			WO 1990-EP1059	W 19900702	

OTHER SOURCE(S): CASREACT 115:71649; MARPAT 115:71649
GI



I

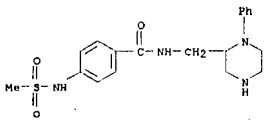


II

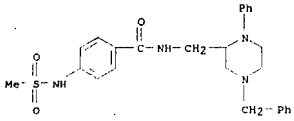
AB Title compds. (I; R = H, alkyl, PhCH2; R1, R2 = alkyl, alkoxy, halo; Z = NR3CO, NR3CH2, OCH2, NR3, NR3SO2; Q = alkylsulfonylimino, Q1; R3 = H, alkyl, allyl, alkoxyalkyl; R4 = H, Me), were prepared as cardiovascular agents, primarily antiarrhythmics (no data). Thus, 4-[(methylsulfonyl)amino]-N-[[4-phenyl-1-(phenylmethyl)piperazin-2-yl]methyl]benzamide hydrochloride was hydrogenolzed in MeOH over Pd(OH)2 to give title compound II.

IT 135036-09-8P 135036-10-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antiarrhythmic)

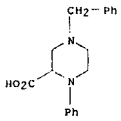
RN 135036-09-8 CAPLUS
CN Benzamide, 4-[(methylsulfonyl)amino]-N-[(1-phenyl-2-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



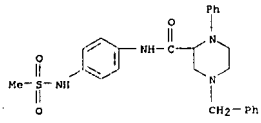
RN 135036-10-1 CAPLUS
CN Methanesulfonamide, N-[4-[[(1-phenyl-2-piperazinyl)methyl]amino]phenyl]- (9CI) (CA INDEX NAME)



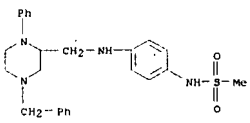
RN 135036-33-8 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

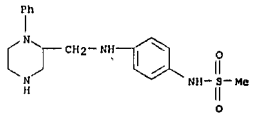


RN 135036-42-9 CAPLUS
CN 2-Piperazinecarboxamide, N-[4-[(methylsulfonyl)amino]phenyl]-1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



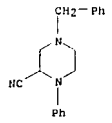
RN 135036-43-0 CAPLUS
CN Methanesulfonamide, N-[4-[[[1-phenyl-4-(phenylmethyl)-2-piperazinyl]methyl]amino]phenyl]- (9CI) (CA INDEX NAME)



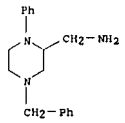


IT 135036-22-5P 135036-23-6P 135036-24-7P
135036-33-8P 135036-42-9P 135036-43-0P
135063-15-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for antiarrhythmic)

RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

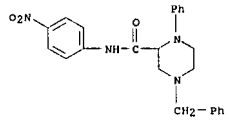


RN 135036-23-6 CAPLUS
CN 2-Piperazinemethanamine, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



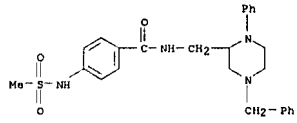
RN 135036-24-7 CAPLUS
CN Benzamide, 4-[(methylsulfonyl)amino]-N-[[1-phenyl-4-(phenylmethyl)-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)

RN 135063-15-9 CAPLUS
CN 2-Piperazinecarboxamide, N-(4-nitrophenyl)-1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



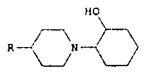
IT 135036-24-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of antiarrhythmic)

RN 135036-24-7 CAPLUS
CN Benzamide, 4-[(methylsulfonyl)amino]-N-[[1-phenyl-4-(phenylmethyl)-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 63 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:231402 CAPLUS
DOCUMENT NUMBER: 110:231402
TITLE: Synthesis, in vitro acetylcholine-storage-blocking activities, and biological properties of derivatives and analogs of trans-2-(4-phenylpiperidino)cyclohexanol (vesamicol)
AUTHOR(S): Rogers, Gary A.; Parsons, Stanley M.; Anderson, D. C.; Nilsson, Lena M.; Bahr, Ben A.; Kornreich, Wayne D.; Kaufman, Rose; Jacobs, Robert S.; Kirtman, Bernard
CORPORATE SOURCE: Dep. Chem., Univ. California, Santa Barbara, CA, 93106, USA
SOURCE: Journal of Medicinal Chemistry (1989), 32(6), 1217-30
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:231402
GI



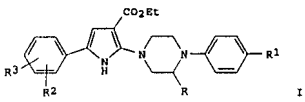
AB Eighty-four analogs, e.g., I [R = (un)substituted Ph, cyclohexyl, PhCH2, Ph(CH2)3] and derivs. of the acetylcholine storage-blocking drug trans-2-4(4-phenylpiperidino)cyclohexanol (vesamicol) were synthesized, and their potencies were evaluated with the acetylcholine active-transport assay utilizing purified synaptic vesicles from Torpedo elec. organ. The parent drug exhibits enantioselectivity, with (-)-vesamicol being 25-fold more potent than (+)-vesamicol. The mol. structure and absolute configuration of (+)-vesamicol were determined by x-ray crystallog. The absolute configuration
of (-)-vesamicol is (1R,2R). Structure-activity evidence indicates that (-)-vesamicol does not act as an acetylcholine analog. Alterations to all three rings can have large effects on potency. Unexpectedly, analogs locking the alc. and ammonium groups trans-diequatorial or trans-diaxial both exhibit good potency. A potent benzovesamicol family was discovered that is suitable for facile elaboration of the sort useful in affinity labeling and affinity chromatog. applications. A good correlation was found between potencies as assessed by the acetylcholine transport assay and LD50 values in mouse.

IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with cyclohexene epoxide)

RN 2946-76-1 CAPLUS

CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 64 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:189237 CAPLUS
DOCUMENT NUMBER: 110:189237
TITLE: Synthesis and antimicrobial activity of some pyrrole derivatives. III. 2-(4-Arylpiperazino)-3-ethoxycarbonyl-5-arylpyrrole derivatives
AUTHOR(S): Cocco, M. T.; Congiu, C.; Maccioni, A.; Schivo, M. L.; De Logu, A.; Palmieri, G.
CORPORATE SOURCE: Ist. Chim. Farm. Tossicol. Appl., Univ. Cagliari, Cagliari, Italy
SOURCE: Farmaco, Edizione Scientifica (1988), 43(12), 951-60
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

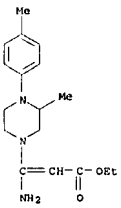


AB The synthesis of the title compds. (I, R = H, Me; R1 = H, halo; R2 =H, OMe, halo, NO2, alkyl; R3 = halo, Me, OMe) is described. The in vitro biol. investigation showed that I (R = R1 H; R2 = 3-NO2; R3 = 4-Cl) had considerable antibacterial activity against gram-pos. microorganisms and antifungal activity against Candida rugosa, while the other I did not show significant activity.

IT 120244-18-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

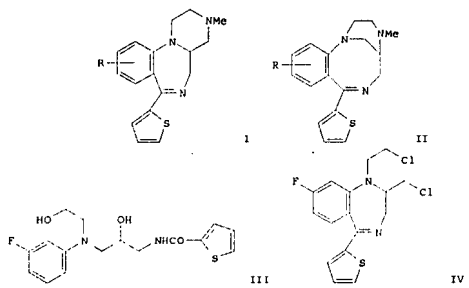
RN 120244-18-0 CAPLUS

CN 2-Propenoic acid, 3-amino-3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]-, ethyl ester (CA INDEX NAME)



L9 ANSWER 65 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:173198 CAPLUS
DOCUMENT NUMBER: 110:173198
TITLE: 1,4-Benzodiazepines and 1,5-benzodiazocines. X1. Synthesis and biological activity
AUTHOR(S): Heitmann, Walter; Liepmann, Hans; Maetzel, Uwe; Zeugner, Horst; Fuchs, Andreas M.; Kraehling, Hermann; Ruhland, Michael; Mol, Frans; Tulp, Martin T. M.
CORPORATE SOURCE: Pharm. Div., Kali-Chemie A.-G., Hannover, D-3000, Fed. Rep. Ger.
SOURCE: European Journal of Medicinal Chemistry (1988), 23(3), 249-56
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 110:173198
GI

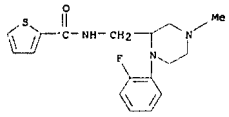


AB The pyrazinobenzodiazepine derivs. I (R = 9-, 10-, 11-F, 11-Me, 11-MeO) and (iminoethano)benzodiazocine derivs. II (R = 7-, 8-, 9-F) were prepared Thus, the amide III was cyclized by POCl3 to give the benzodiazepine IV, which was cyclized with MeNH2 to give I (R = 10-F). I and II exhibited pronounced antipsychotic activity. The influence of fluorosubstitution and variation of the fused ring system were measured.

IT 120107-24-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization reaction of, pyrazinobenzodiazepine derivative from)

RN 120107-24-6 CAPLUS

CN 2-Thiophenecarboxamide, N-[[1-(2-fluorophenyl)-4-methyl-2-piperazinyl]methyl]-, dihydrochloride (9CI) (CA INDEX NAME)

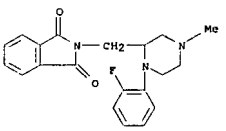


●2 HCl

IT 120107-04-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and hydrazonolysis of)

RN 120107-04-2 CAPLUS

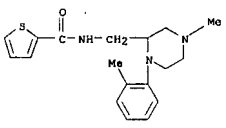
CN 1H-Isoindole-1,3(2H)-dione, 2-[[1-(2-fluorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



IT 120107-10-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and intramol. cyclization of, pyrazinobenzodiazepine derivative from)

RN 120107-10-0 CAPLUS

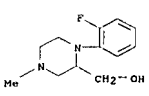
CN 2-Thiophenecarboxamide, N-[[4-methyl-1-(2-methylphenyl)-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



IT 120107-03-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and mesylation of)

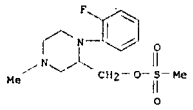
RN 120107-03-1 CAPLUS

CN 2-Piperazinemethanol, 1-(2-fluorophenyl)-4-methyl- (9CI) (CA INDEX NAME)

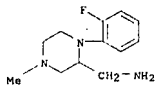


IT 120107-22-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

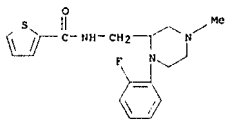
(preparation and reaction with potassium phthalimide)
RN 120107-22-4 CAPLUS
CN 2-Piperazinemethanol, 1-(2-fluorophenyl)-4-methyl-, methanesulfonate (ester) (9CI) (CA INDEX NAME)



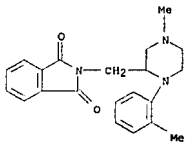
IT 120107-23-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with thiophenecarbonyl chloride)
RN 120107-23-5 CAPLUS
CN 2-Piperazinemethanamine, 1-(2-fluorophenyl)-4-methyl- (9CI) (CA INDEX NAME)



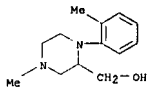
IT 120107-05-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 120107-05-3 CAPLUS
CN 2-Thiophenecarboxamide, N-[[1-(2-fluorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



IT 120107-09-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, hydrazinolysis, and reaction with thiophenecarbonyl chloride)
RN 120107-09-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[[4-methyl-1-(2-methylphenyl)-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



IT 120107-08-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, mesylation, and reaction with potassium phthalimide)
RN 120107-08-6 CAPLUS
CN 2-Piperazinemethanol, 4-methyl-1-(2-methylphenyl)- (9CI) (CA INDEX NAME)

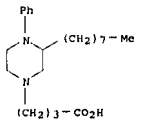


L9 ANSWER 66 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:601296 CAPLUS
DOCUMENT NUMBER: 109:201296
TITLE: Photographic material for light-stable images
INVENTOR(S): Yoshimoto, Shinji; Nakagawa, Satoshi; Kaneko, Yutaka; Sugita, Shuichi; Shimada, Naoko
PATENT ASSIGNEE(S): Konica Co., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63101848	A	19880506	JP 1986-246728	19861017 <--
PRIORITY APPLN. INFO.:			JP 1986-246728	19861017

GI For diagram(s), see printed CA Issue.
AB A Ag halide photog. material contains ≥1 magenta couples I [Z = atom required to complete N heterocycle; X = H, group releasable on reacting with oxidized form of color developing agent; R = H, substituent] and an image stabilizer II [R21 = SO3M, CO2M; M = H, monovalent metal; X = divalent organic group; Z = atoms required to form 5-7-membered N heterocycle]. Light-stable images are obtained and staining and fogging are minimized.
IT 117209-45-7

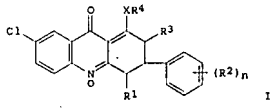
RL: USES (Uses)
(magenta image stabilizer, for light stability)
RN 117209-45-7 CAPLUS
CN 1-Piperazinebutanoic acid, 3-octyl-4-phenyl- (9CI) (CA INDEX NAME)



L9 ANSWER 67 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:473142 CAPLUS
DOCUMENT NUMBER: 109:73142
TITLE: New 1-substituted 3-aryl-7-chloro-3,4-dihydro-2H-acridone N-oxides, a procedure for their preparation, formulations containing them, and their use as pharmaceuticals and feed additives
INVENTOR(S): Dhar, Rajkumar; Venugopalan, Bindumadhavan; Chatterjee, Dipak Kumar; Rupp, Richard Helmut; De Souza, Noel John
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 9 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

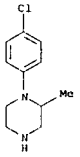
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3624702	A1	19880204	DE 1986-3624702	19860722 <--
IN 164921	A1	19890708	IN 1986-BO149	19860515 <--
EP 254224	A2	19880127	EP 1987-110365	19870717 <--
EP 254224	A3	19890419		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8705297	A	19880330	ZA 1987-5297	19870720 <--
US 4803204	A	19890207	US 1987-75643	19870720 <--
DK 8703802	A	19880123	DK 1987-3802	19870721 <--
JP 63033365	A	19880213	JP 1987-180207	19870721 <--
HU 44516	A2	19880328	HU 1987-3360	19870721 <--
AT 8702609	A	19881215	AT 1987-2609	19871008 <--
AT 388553	B	19890725		
PRIORITY APPLN. INFO.:			DE 1986-3624702 A	19860722
OTHER SOURCE(S):	MARPAT 109:73142			

GI



I

AB The title compds. I [R1,R3 = H, alkyl, carbalkoxy, Ph (un)substituted with alkyl, halo, or NH2; R2 = halo, CF3; n = 0-3; X = O, N; when X = O, R4= alkyl; when X = N, XR4 = dialkylamino, 5- or 6-membered heterocyclyl optionally containing another heteroatom, optionally substituted with (un)substituted alkyl or Ph (un)substituted with alkyl, alkoxy, or halo], having high activity against the pathogens of malaria and coccidiosis, were prepared A suspension of 7-chloro-3,4-dihydro-10-hydroxy-3-(4-trifluoromethylphenyl)-1,9(2H,10H)-acridinedione in MeOH was treated dropwise with pyrrolidine at room temperature to give 78% I [R1 = R3 = H, (R2)n = 4-CF3, XR4 = pyrrolidine]. At 10-25 mg I/ kg + S in mice infected with Plasmodium berghei, complete healing was achieved.
IT 55117-80-1, 1-(4-Chlorophenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(aminolysis by, of hydroxyacridinedione derivative)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)

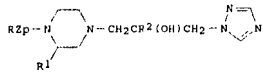


L9 ANSWER 68 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:620995 CAPLUS
DOCUMENT NUMBER: 105:220995
TITLE: Piperazinylmethyl-1,2,4-triazolylmethylcarbinol fungicide
INVENTOR(S): Holmwood, Graham; Buechel, Karl Heinz; Brandes, Wilhelm; Reinecke, Paul
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 44 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3508909	A1	19860918	DE 1985-3508909	19850313 <--
US 4738962	A	19880419	US 1986-832502	19860221 <--
EP 198191	A1	19861022	EP 1986-102767	19860303 <--
EP 198191	B1	19890906		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 46152	T	19890915	AT 1986-102767	19860303 <--
AU 8654433	A	19861016	AU 1986-54433	19860307 <--
JP 61212568	A	19860920	JP 1986-51578	19860311 <--
DD 243848	A5	19870318	DD 1986-287770	19860311 <--
DK 8601144	A	19860914	DK 1986-1144	19860312 <--
BR 8601052	A	19861125	BR 1986-1052	19860312 <--
ZA 8601843	A	19861126	ZA 1986-1843	19860312 <--
HU 42280	A2	19870728	HU 1986-1060	19860313 <--
ES 552966	A1	19871101	ES 1986-552966	19860313 <--
PRIORITY APPLN. INFO.:			DE 1985-3508909 A	19850313
			EP 1986-102767 A	19860303

OTHER SOURCE(S): CASREACT 105:220995

GI



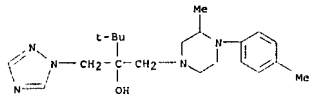
I

AB The title compds. I (R = substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkalkyl, aryloxyalkyl, arylthioalkyl; R1 = H, alkyl; R2 = substituted alkyl, alkenyl, cycloalkyl, aryl heterocyclyl; Z = CO, SO2; p = 0,or 1) are prepared as agricultural and medical fungicides. Thus, 16.7 g 2-tert-butyl-1-(1,2,4-triazol-1-yl)methyloxirane, 16.2 g 1-phenylpiperazine and 150 mL EtOH was refluxed for 15 h to give 19 g 3,3-dimethyl-2-[1-(4-phenylpiperazin-1-yl)-methyl]-1-(1,2,4-triazol-1-yl)buten-2-ol. I are active against Pyrenophora teres on barley and Uromyces appendiculatus on bean. I are also medical virucides.

IT 105411-76-5P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as fungicide)

RN 105411-76-5 CAPLUS

CN 1-Piperazineethanol, α-(1,1-dimethylethyl)-3-methyl-4-(4-methylphenyl)-α-(1H-1,2,4-triazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 69 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:566904 CAPLUS
DOCUMENT NUMBER: 105:166904
TITLE: Herbicide antidote
INVENTOR(S): Foery, Werner; Nyffeler, Andreas; Gerber, Hans Rudolf; Martin, Henry
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 143 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 190105	A2	19860806	EP 1986-810046	19860127 <--
EP 190105	A3	19881026		
R: BE, CH, DE, FR, GB, IT, LI, NL				
CA 1278695	C	19910108	CA 1986-500569	19860129 <--
BR 8600383	A	19861014	BR 1986-383	19860130 <--
JP 61176504	A	19860808	JP 1986-20005	19860131 <--
PRIORITY APPLN. INFO.:			CH 1985-418 A	19850131

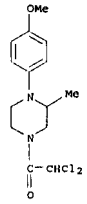
OTHER SOURCE(S): MARPAT 105:166904

AB The dichloroacetamides RR1NCOCHCl2 (R,R1 = H, (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, etc.; NRR1 = heterocyclic radical) are prepared as antidotes for the N-(2-methoxycarbonylphenylsulfonyl)-N-(4,6-bisdifluoromethoxypyrimidin-2-yl)urea (I) herbicide. Thus, condensation of N-(3,4-dimethoxybenzyl)-N-isopropylamine (preparation given) with Cl2CHCOCl, in NaOH-containing MePh, at -10 to -15°, gave N-(3,4-dimethoxybenzyl)-N-iso-Pr dichloroacetanilide. When (H2C:CHCH2)2NCOCHCl2 (200 g/ha) was applied to corn in tank mixture with 400 g I/ha, 75% protection against the phytotoxicity of I to the crop was observed

IT 104767-29-5P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antidote for sulfonylurea herbicide)

RN 104767-29-5 CAPLUS

CN Piperazine, 4-(dichloroacetyl)-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



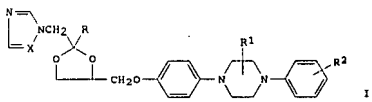
L9 ANSWER 70 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:132069 CAPLUS
DOCUMENT NUMBER: 102:132069
TITLE: [[4-[4-(4-Phenyl-1-piperazinyl)phenoxymethyl]-1,3-dioxolan-2-yl]methyl]-1H-imidazoles and 1H-1,2,4-triazoles
INVENTOR(S): Heeres, Jan; Stokbroekx, Raymond A.; Backx, Leo J. J.
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: Eur. Pat. Appl., 113 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 118138	A1	19840912	EP 1984-200092	19840124 <--
EP 118138	B1	19890614		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4619931	A	19861028	US 1984-569122	19840109 <--
AT 44030	T	19890615	AT 1984-200092	19840124 <--
CA 1271194	A1	19900703	CA 1984-447194	19840210 <--
JP 59172486	A	19840929	JP 1984-32768	19840224 <--
JP 07042285	B	19950510		
DK 8401070	A	19840829	DK 1984-1070	19840227 <--
DK 164454	B	19920629		
DK 164454	C	19921109		
FI 8400781	A	19840829	FI 1984-781	19840227 <--
FI 82043	B	19900928		
FI 82043	C	19910110		
NO 8400735	A	19840829	NO 1984-735	19840227 <--
NO 160138	B	19881205		
NO 160138	C	19890315		
AU 8425097	A	19840906	AU 1984-25097	19840227 <--
AU 559461	B2	19870312		
ZA 8401449	A	19851030	ZA 1984-1449	19840227 <--
IL 71066	A	19871220	IL 1984-71066	19840227 <--
ES 530138	A1	19850516	ES 1984-530138	19840228 <--
ES 530140	A1	19850601	ES 1984-530140	19840228 <--
ES 530139	A1	19850901	ES 1984-530139	19840228 <--
US 4735942	A	19880405	US 1986-869537	19860602 <--
NO 8702221	A	19840829	NO 1987-2221	19870527 <--
NO 163817	B	19900417		
NO 163817	C	19900725		
US 4861879	A	19890829	US 1988-154173	19880209 <--
CA 1309412	C2	19921027	CA 1989-615528	19891025 <--
FI 84058	B	19910628	FI 1989-5089	19891026 <--
FI 84058	C	19911010		
NO 9000396	A	19840829	NO 1990-396	19900129 <--
NO 173866	B	19931108		
NO 173866	C	19940216		
JP 05246999	A	19930924	JP 1991-24132	19910124 <--
JP 07064823	B	19950712		
DK 9100783	A	19910429	DK 1991-783	19910429 <--
DK 9101088	A	19910607	DK 1991-1088	19910607 <--
DK 166673	B1	19930628		
PRIORITY APPLN. INFO.:			US 1983-470405 A	19830228

	US 1984-569122	A	19840109
	EP 1984-200092	A	19840124
	CA 1984-447194	A3	19840210
	FI 1984-781	A	19840227
	NO 1984-735	A1	19840227
	US 1986-869537	A3	19860602

OTHER SOURCE(S): CASREACT 102:132069; MARPAT 102:132069

GI



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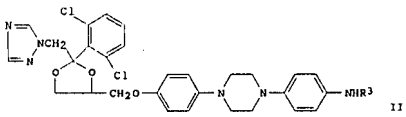


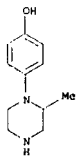
II

AB Over 300 title compds. I [R = (un)substituted Ph; R1 = H, alkyl; R2 = urea, thiourea, amido, 5-membered N-containing heterocycle; X = N, CH] and their intermediates, useful as pharmaceutical fungicides, were prepared Thus, aniline derivative II (R3 = H) was treated with ClCO2Ph to give II (R3 = CO2Ph). At 2.5 mg/kg orally, daily for 3 days in rats, II (R3 = CO2Ph) controlled Candida albicans at the 14th day after infection.

IT 95182-89-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of)

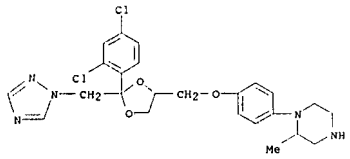
RN 95182-89-1 CAPLUS

CN Phenol, 4-(2-methyl-1-piperazinyl)-, dihydrobromide (9CI) (CA INDEX NAME)

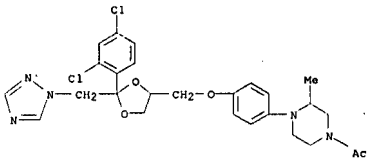


●2 HBr

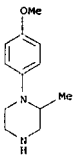
IT 95182-92-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and arylation of)
RN 95182-92-6 CAPLUS
CN Piperazine, 1-[4-[[2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-2-methyl- (9CI) (CA INDEX NAME)



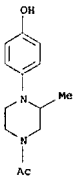
IT 95182-91-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deacylation of)
RN 95182-91-5 CAPLUS
CN Piperazine, 4-acetyl-1-[4-[[2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-2-methyl- (9CI) (CA INDEX NAME)



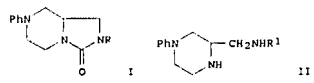
IT 35947-12-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



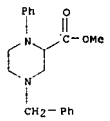
IT 95182-90-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with dioxolanemethanol derivative)
RN 95182-90-4 CAPLUS
CN Piperazine, 4-acetyl-1-(4-hydroxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 71 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:490876 CAPLUS
DOCUMENT NUMBER: 101:90876
TITLE: Hexahydroimidazo[1,5-a]pyrazines. II. Synthesis of 7-phenyl-1,5,6,7,8,8a-hexahydroimidazo[1,5-a]pyrazin-3(2H)-one and derivatives
AUTHOR(S): Toja, E.; Omodei-Sale, A.; Corsico, N.
CORPORATE SOURCE: Lab. Ric., Gruppo Lepetit S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1984), 39(5), 450-62
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian
OTHER SOURCE(S): CASREACT 101:90876
GI

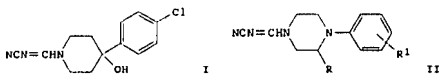


AB Title compds. I (R = Ph, tolyl, ClC6H4, anisyl, Me, allyl), useful as central nervous system depressants, were prepared from piperazines II (R1 = Ph, tolyl, ClC6H4 anisyl, H). A mixture of II (R1 = H) and 1,1'-carbonyldiimidazole in THF was kept 11 days at room temperature, and the product was treated with NaH and MeI in DMF to give I (R = Me).
IT 91532-79-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 91532-79-5 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)

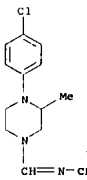


L9 ANSWER 72 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:490874 CAPLUS
DOCUMENT NUMBER: 101:90874
TITLE: Antimycotic agents, XVI. Halogenated (cyanaminomethylene)piperidines and -piperazines
AUTHOR(S): Kreutzberger, Alfred; Kreutzberger, Elfriede
CORPORATE SOURCE: Inst. Pharm., Johannes Gutenberg-Univ., Mainz, 6500,

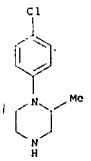
Fed. Rep. Ger.
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1984), 317(5), 417-20
CODEN: ARPMAS; ISSN: 0365-6233
DOCUMENT TYPE: Journal
LANGUAGE: German
GI



AB Aminomethylating H2NCN with s-trazine in the presence of secondary amines gave cyanomethylene heterocycles I and II [R = Me, R1 = p-Cl; R = H, R1 = p-F, m-F3C, 4,3-Cl(F3C)], classed as dehydro-N-Mannich bases. I and II [R1 = 4,3-Cl(F3C)] showed antimycotic activity (no data).
IT 91126-05-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 91126-05-5 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-4-[(cyanoimino)methyl]-2-methyl- (9CI) (CA INDEX NAME)



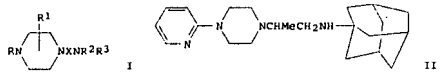
IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cyanamide and triazine)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 73 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:423499 CAPLUS
DOCUMENT NUMBER: 101:23499
TITLE: Piperazine derivatives with anticholinergic and antihistaminic activity
INVENTOR(S): Milani, Carlo; Carminati, Giovanni Maria; Sovera, Attilio
PATENT ASSIGNEE(S): Selvi e C. S.p.A., Italy
SOURCE: Belg., 49 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
BE 897828	A2	19840116	BE 1983-60212	19830927	<--
US 4457931	A	19840703	US 1982-424512	19820927	<--
ZA 8306949	A	19840530	ZA 1983-6949	19830919	<--
JP 59089665	A	19840523	JP 1983-176190	19830922	<--
JP 61039289	B	19860903			
FR 2533564	A1	19840330	FR 1983-15172	19830923	<--
FR 2533564	B1	19861003			
DE 3334757	A1	19840329	DE 1983-3334757	19830926	<--
ES 525953	A1	19860201	ES 1983-525953	19830926	<--
AT 8303412	A	19880915	AT 1983-3412	19830926	<--
AT 387964	B	19890410			
NL 8303311	A	19840416	NL 1983-3311	19830927	<--
GB 2135991	A	19840912	GB 1983-25839	19830927	<--
GB 2135991	B	19851204			
ES 542946	A1	19860101	ES 1985-542946	19850416	<--
ES 542947	A1	19860101	ES 1985-542947	19850416	<--

PRIORITY APPLN. INFO.: US 1982-424512 A 19820927
OTHER SOURCE(S): CASREACT 101:23499; MARPAT 101:23499
GI



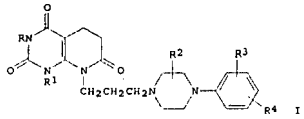
I II

IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with chloroethylmorpholine)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 74 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:407184 CAPLUS
DOCUMENT NUMBER: 101:7184
TITLE: Pyridopyrimidinetriones, their use, and drugs containing them
INVENTOR(S): Klemm, Kurt; Pruesse, Wolfgang; Baron, Lothar; Kilian, Ulrich; Sanders, Karl
PATENT ASSIGNEE(S): Byk-Gulden Lomberg Chemische Fabrik G.m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 50 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 3326118	A1	19840209	DE 1983-3326118	19830720	<--

PRIORITY APPLN. INFO.: CH 1982-4651 A 19820802
OTHER SOURCE(S): MARPAT 101:7184
GI



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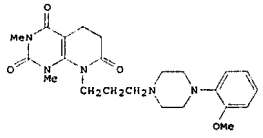
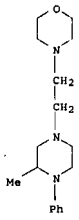
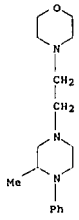


II

AB Aminoalkylpiperazines I (X = alkylene; R = aryl, aralkyl, heterocyclic; R1 = H, alkyl; R2, R3 = H, alkyl, cycloalkyl, aryl; NR2R3 = heterocyclic) were prepared Thus, 1-(2-pyridyl)piperazine was treated with BrCHMeCH2CO2Et and the resulting ester reduced to the alc., brominated, and aminated with 1-adamantylamine to give II. II had an anticholinergic ED50 in vitro of 0.001 μg/mL.
IT 90476-58-7P 90476-80-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and anticholinergic and antihistaminic activity of)
RN 90476-58-7 CAPLUS
CN Morpholine, 4-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

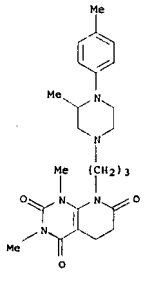


RN 90476-80-5 CAPLUS
CN Morpholine, 4-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]-, trihydrochloride (9CI) (CA INDEX NAME)

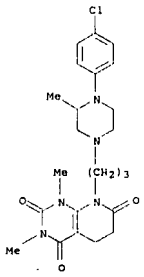


●3 HCl

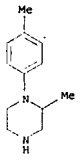
AB Title compds. (I) (R = H, C1-5 alkyl; R1 = C1-5 alkyl; R2 = H, C1-3 alkyl; R3 = H, halo, C1-4 alkyl or alkoxy, CF3; R4 = H, halo, C1-4 alkyl or alkoxy) and their N-oxides and salts were prepared and shown to have antihypertensive activity. Thus, 6-[[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]amino]-1,3-dimethyluracil was added to CH2:CHCO2Et, and the product saponified, then cyclized by heating 1 h at 140°/12-15 mbar to give the pyridopyrimidinetrione II.
IT 89989-10-6P 89989-11-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antihypertensive)
RN 89989-10-6 CAPLUS
CN Pyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione, 5,8-dihydro-1,3-dimethyl-8-[3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



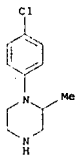
RN 89989-11-7 CAPLUS
CN Pyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione, 8-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propyl]-5,8-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



IT 35947-11-6 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (chloropropyl)pyridopyrimidinetrione derivs.)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 75 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:85510 CAPLUS
DOCUMENT NUMBER: 100:85510
TITLE: Theophylline derivatives as cerebral circulation improvers
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 58150511	A	19830907	JP 1982-31686	19820302 <--
PRIORITY APPLN. INFO.:			JP 1982-31686	19820302

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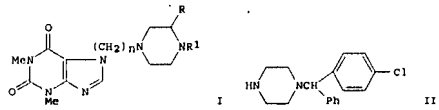
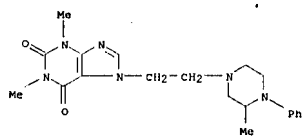
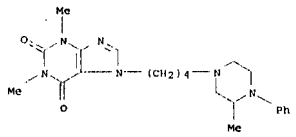


AB Ninety-five theophyllines I (R = H, Me; R1 = aryl, Ph2CH, pyridyl; n = 2-10) were prepared and were effective cerebral vasodilators at 0.1-10 μg/kg. Thus, refluxing 7-(2-bromoethyl)theophylline 6.3, piperazine II 5.7, and Et3N 4.0 g in C6H6 18.5 h gave 42.5% I.HCl (R = H, R1 = p-chlorobenzhydryl, n = 2).
IT 81996-76-1P 81996-77-2P 81996-78-3P
81996-79-4P 81996-80-7P 81996-84-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 81996-76-1 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

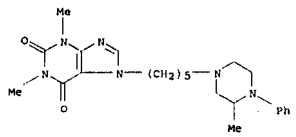


RN 81996-77-2 CAPLUS

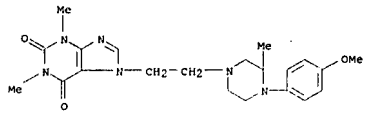
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



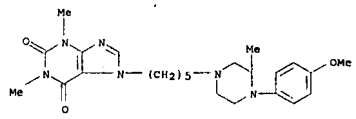
RN 81996-78-3 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[5-(3-methyl-4-phenyl-1-piperazinyl)pentyl]- (9CI) (CA INDEX NAME)



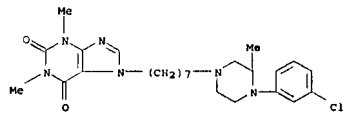
RN 81996-79-4 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 81996-80-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[5-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]pentyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 81996-84-1 CAPLUS
CN 1H-Purine-2,6-dione, 7-[7-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]heptyl]-3,7-dihydro-1,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

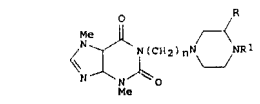


● HCl

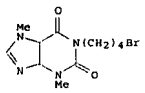
L9 ANSWER 76 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:68315 CAPLUS
DOCUMENT NUMBER: 100:68315
TITLE: Theobromine derivatives as brain circulation improvers
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 58148820	A	19830905	JP 1982-29043	19820226 <--
PRIORITY APPLN. INFO.:			JP 1982-29043	19820226

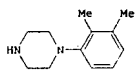
GI



I



II



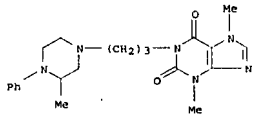
III

AB Fifty-five theobromine derivs. (I; R = H, alkyl; R1 = aryl, benzhydryl; n = 2-10) and their acid adducts, effective brain circulation improvers at 0.1-10 μg/kg, were prepared Thus, a mixture of theobromine derivative II 9.5, piperazine derivative III 3.8, and Et3N 4.0 g in MePh was refluxed 13 h to give 41.6% I (R = H, R1 = 2,3-xylyl, n = 4).

IT 81995-72-4P 81995-73-5P 81995-74-6P
81995-75-7P 81995-76-8P 81995-77-9P
81995-78-0P 81997-11-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

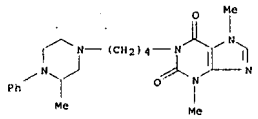
RN 81995-72-4 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



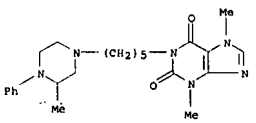
RN 81995-73-5 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



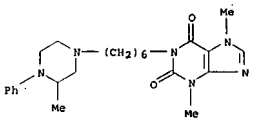
RN 81995-74-6 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[5-(3-methyl-4-phenyl-1-piperazinyl)pentyl]- (9CI) (CA INDEX NAME)



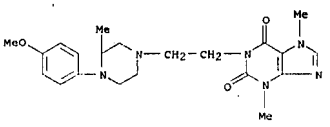
RN 81995-75-7 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[6-(3-methyl-4-phenyl-1-piperazinyl)hexyl]- (9CI) (CA INDEX NAME)



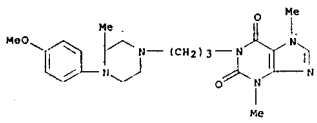
RN 81995-76-8 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



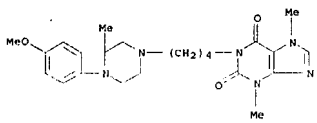
RN 81995-77-9 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



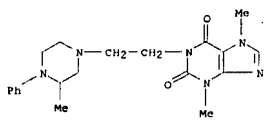
RN 81995-78-0 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[4-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]butyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



RN 81997-11-7 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 77 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:600512 CAPLUS

DOCUMENT NUMBER: 99:200512

TITLE: Composition for the treatment of pain, fever, tissue and/or bone and joint inflammation, containing theobromine or theophylline derivatives as active constituents

INVENTOR(S): Kaneko, Takeru; Ozaki, Satoru; Takizawa, Kimie; Sugimoto, Hachiro

PATENT ASSIGNEE(S): Eisai Co., Ltd. , Japan

SOURCE: Ger. Offen., 80 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

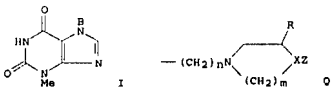
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
DE 3307395	A1	19830908	DE 1983-3307395		19830302	<--
JP 58148818	A	19830905	JP 1982-31684		19820302	<--
JP 01018050	B	19890403				
JP 58148819	A	19830905	JP 1982-31685		19820302	<--
JP 01013689	B	19890307				
EP 87810	A1	19830907	EP 1983-102019		19830302	<--
EP 87810	B1	19860625				
R: BE, CH, DE, FR, GB, IT, LI, NL, SE						
US 4543254	A	19850924	US 1983-471564		19830302	<--
US 4599337	A	19860708	US 1985-755404		19850716	<--
PRIORITY APPLN. INFO.:			JP 1982-31684	A	19820302	
			JP 1982-31685	A	19820302	
			US 1983-471564	A3	19830302	

OTHER SOURCE(S): CASREACT 99:200512; MARPAT 99:200512

GI



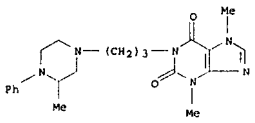
I Q

AB I, in which one of A and B is Me and the other is Q (R is H or lower alkyl; Z is C6H3X1X2 [X1 and X2 are H, lower alkyl or alkoxy, F3C, or halogen], pyridyl, or CH(C6H4Y1)(C6H4Y2) [Y1 and Y2 are H, lower alkyl or alkoxy, F3C, or halogen]; X is N or C, m is 2 or 3, and n is 2-10) are analgesics, antipyretics, and inflammation inhibitors. Analgesic activity (ED50), LD50, and LD50/ED50 ratio values of representative compds. in mice and rats, antipyretic, and antiphlogistic activities are reported. Thus, 7-(2-bromoethyl)theophylline [23146-05-6] and 1-(p-chlorobenzhydryl)piperazine [303-26-4] were refluxed with Et3N in C6H6, the Et3N.HCl obtained was filtered, the filtrate was extracted with dilute HCl, made alkaline and extracted with CHCl3. The extract was washed, dried, evaporated, and the crystals were converted to the HCl salt and recrystd. from Me Cellosolve-H2O to obtain 7-[2-[4-(p-chlorobenzhydryl)piperazinyl]ethyl]theophylline-2HCl [82013-70-5]. Formulation of tablets and capsules with typical excipients is described.

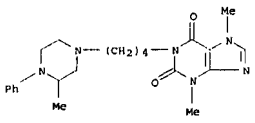
IT 81995-72-4P 81995-73-5P 81995-74-6P
81995-75-7P 81995-76-8P 81995-77-9P
81995-78-0P 81996-76-1P 81996-77-2P
81996-79-4P 81996-80-7P 81996-84-1P
81997-11-7P 87798-78-5P
RL: THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, for analgesics and antipyretics and inflammation inhibitors)

RN 81995-72-4 CAPLUS

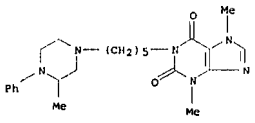
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



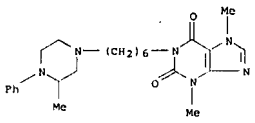
RN 81995-73-5 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



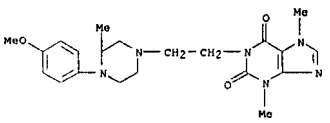
RN 81995-74-6 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[5-(3-methyl-4-phenyl-1-piperazinyl)pentyl]- (9CI) (CA INDEX NAME)



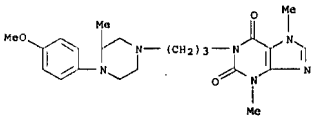
RN 81995-75-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[6-(3-methyl-4-phenyl-1-piperazinyl)hexyl]- (9CI) (CA INDEX NAME)



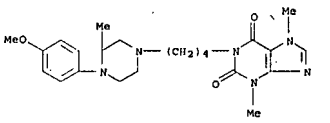
RN 81995-76-8 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



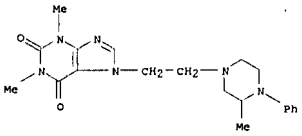
RN 81995-77-9 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



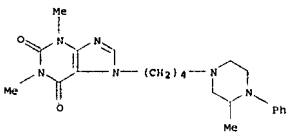
RN 81995-78-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[4-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]butyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



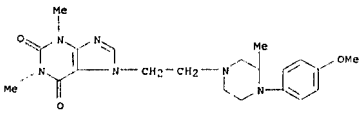
RN 81996-76-1 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



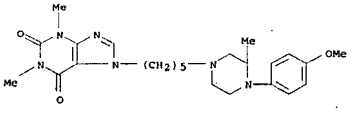
RN 81996-77-2 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



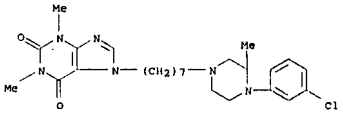
RN 81996-79-4 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 81996-80-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[5-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]pentyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)

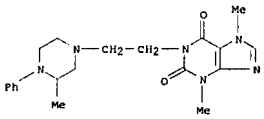


RN 81996-84-1 CAPLUS
CN 1H-Purine-2,6-dione, 7-[7-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]heptyl]-3,7-dihydro-1,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

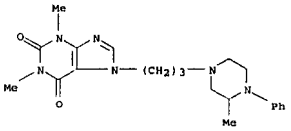


● HCl

RN 81997-11-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



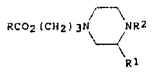
RN 87798-78-5 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 78 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:470678 CAPLUS
DOCUMENT NUMBER: 99:70678
TITLE: Chemistry of 1,3-bifunctional compounds. XXVII. Preparation of 4-N-substituted piperazinyl-1-propyl

esters

AUTHOR(S): Felfoldi, K.; Molnar, A.; Apjok, J.; Czombos, J.; Notheisz, F.; Karpati, E.
CORPORATE SOURCE: Dep. Org. Chem., Jozsef Attila Univ., Szeged, 6720, Hung.
SOURCE: Acta Physica et Chemica (1982), 28(3-4), 225-44
CODEN: AUSHAF; ISSN: 0001-6721
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 99:70678
GI

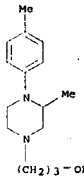


I

AB N-Piperazinepropanol esters I [R = Ph, methoxy-, halo-, or methylphenyl, xanthenyl, methoxycyclohexyl, furyl; R1 = H, Me; R2 = alkyl, alkenyl, cyclohexylmethyl, phenylalkyl, PhOCH2CH2, CO2Et, PhCH:CHCH2, 2,6-Me2C6H3NHCOCH2, Ph, tolyl, Me2C6H3, anisyl, chlorophenyl, F3CC6H4, pyridyl, (un)substituted benzyl] were prepared Some of the above products exhibited antiarrhythmic activity. Thus, 1-(3-hydroxypropyl)-4-isopropylpiperazine was treated with 3-MeOC6H4COCl to give I (R = 3-MeOC6H4, R1 = H, R2 = CHMe2).

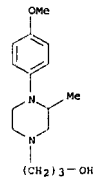
IT 86571-52-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification by, of acid chlorides)

RN 86571-52-0 CAPLUS
CN 1-Piperazinepropanol, 3-methyl-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)



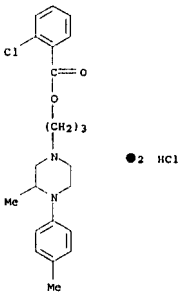
IT 86571-53-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification by, of benzoyl chlorides)

RN 86571-53-1 CAPLUS
CN 1-Piperazinepropanol, 4-(4-methoxyphenyl)-3-methyl- (9CI) (CA INDEX NAME)

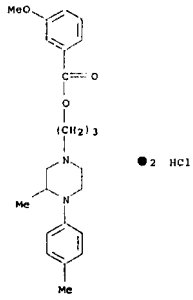


IT 86571-88-2P 86571-89-3P 86571-90-6P
86572-02-3P 86572-03-4P 86585-77-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

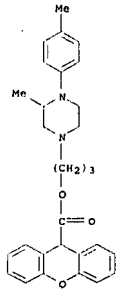
RN 86571-88-2 CAPLUS
CN Benzoic acid, 2-chloro-, 3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)



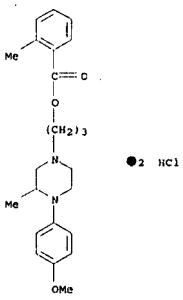
RN 86571-89-3 CAPLUS
CN Benzoic acid, 3-methoxy-, 3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)



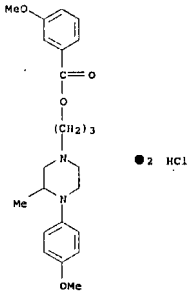
RN 86571-90-6 CAPLUS
CN 9H-Xanthene-9-carboxylic acid, 3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)



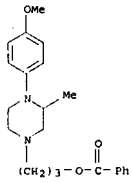
RN 86572-02-3 CAPLUS
CN Benzoic acid, 2-methyl-, 3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)



RN 86572-03-4 CAPLUS
CN Benzoic acid, 3-methoxy-, 3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)

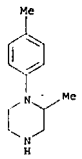


RN 86585-77-5 CAPLUS
CN 1-Piperazinepropanol, 4-(4-methoxyphenyl)-3-methyl-, benzoate (ester), dihydrochloride (9CI) (CA INDEX NAME)

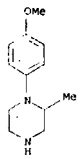


●2 HCl

IT 35947-11-6 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation of, by chloropropanol)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

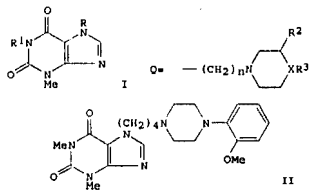


L9 ANSWER 79 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:438769 CAPLUS
DOCUMENT NUMBER: 97:38769
TITLE: Derivatives of theophylline and theobromine
PATENT ASSIGNEE(S): Eisai Co., Ltd. , Japan
SOURCE: Belg., 59 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

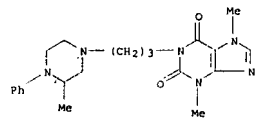
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 890222	A1	19820104	BE 1981-59339	19810904 <--
JP 57046983	A	19820317	JP 1980-121712	19800904 <--
JP 57046984	A	19820317	JP 1980-121713	19800904 <--
JP 63060756	B	19881125		
US 4426383	A	19840117	US 1981-298227	19810831 <--
NL 8104073	A	19820401	NL 1981-4073	19810902 <--
SE 8105240	A	19820305	SE 1981-5240	19810903 <--
SE 456910	B	19881114		
SE 456910	C	19890309		
GB 2083470	A	19820324	GB 1981-26653	19810903 <--
GB 2083470	B	19840912		
DE 3134929	A1	19820609	DE 1981-3134929	19810903 <--
CA 1172632	A1	19840814	CA 1981-385142	19810903 <--
CH 651042	A5	19850830	CH 1981-5675	19810903 <--
FR 2489331	A1	19820305	FR 1981-16855	19810904 <--
FR 2489331	B1	19841130		
US 4564617	A	19860114	US 1983-484044	19830411 <--
SE 8704599	A	19871120	SE 1987-4599	19871120 <--
SE 457083	B	19881128		
SE 457083	C	19890323		

PRIORITY APPLN. INFO.: JP 1980-121712 A 19800904
JP 1980-121713 A 19800904
US 1981-298227 A3 19810831

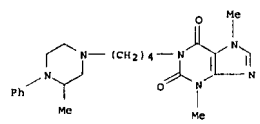
OTHER SOURCE(S): CASREACT 97:38769; MARPAT 97:38769
GI



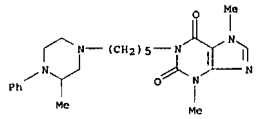
AB The title derivs. I [R, R1 = Me, Q [R2 = H, alkyl; R3 = (un)substituted Ph, (un)substituted diphenylmethyl; X = N, CH; n = 2-10]] were prepared Thus, 7-(4-bromobutyl)theophylline was treated with 1-(o-methoxyphenyl)piperazine to give 37.6% theophylline II. At 0.1 μg/kg the vasodilator II.2 HCl increased the arterial blood flow. I also had central nervous system, antihistaminic, analgesic, antihypertensive, and antiasthmatic activity (no data).
IT 81995-72-4P 81995-73-5P 81995-74-6P
81995-75-7P 81995-76-8P 81995-77-9P
81995-78-0P 81996-76-1P 81996-77-2P
81996-78-3P 81996-79-4P 81996-80-7P
81996-84-1P 81997-11-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 81995-72-4 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



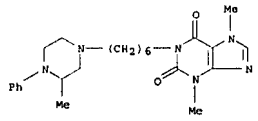
RN 81995-73-5 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



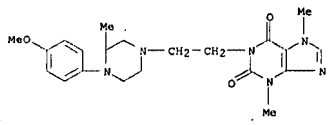
RN 81995-74-6 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[5-(3-methyl-4-phenyl-1-piperazinyl)pentyl]- (9CI) (CA INDEX NAME)



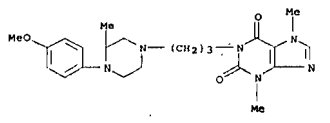
RN 81995-75-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[6-(3-methyl-4-phenyl-1-piperazinyl)hexyl]- (9CI) (CA INDEX NAME)



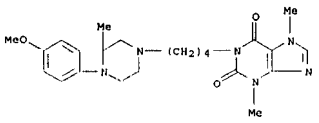
RN 81995-76-8 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



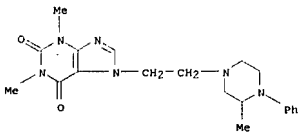
RN 81995-77-9 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



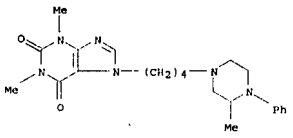
RN 81995-78-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[4-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]butyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



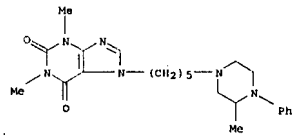
RN 81996-76-1 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



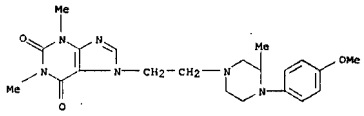
RN 81996-77-2 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



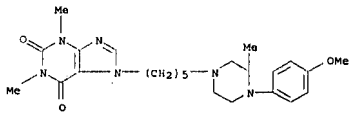
RN 81996-78-3 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[5-(3-methyl-4-phenyl-1-piperazinyl)pentyl]- (9CI) (CA INDEX NAME)



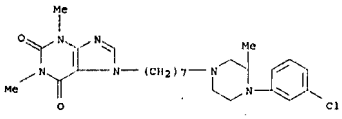
RN 81996-79-4 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 81996-80-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[5-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]pentyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)

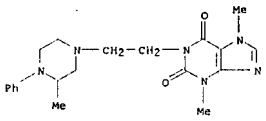


RN 81996-84-1 CAPLUS
CN 1H-Purine-2,6-dione, 7-[7-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]heptyl]-3,7-dihydro-1,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

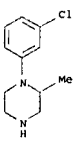


● HCl

RN 81997-11-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

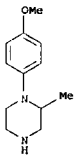


IT 75348-33-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (haloalkyl)theophylline)
RN 75348-33-3 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



IT 2946-76-1 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (haloalkyl)theophylline and (bromoalkyl)theobromine)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

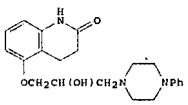
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 80 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:491203 CAPLUS
DOCUMENT NUMBER: 95:91203
TITLE: Central nervous system depressants
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 48 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 56046812	A	19810428	JP 1979-124878	19790927 <--
JP 02012204	B	19900319		
PRIORITY APPLN. INFO.:			JP 1979-124878	A 19790927

GI



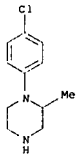
● HCl

I

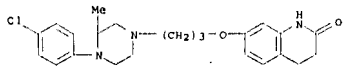
AB 5-[2-Hydroxy-3-(4-phenylpiperazinyl)propoxy]-3,4-dihydrocarbostyril-HCl (I) [72566-28-0] and its analogs are central nervous system depressants.

Thus, I and its analogs increased the anesthetic effect of halothane in mice. I was synthesized by treating 5-(2,3-epoxypropoxy)-3,4-dihydrocarbostyril [51781-14-7] with 4-phenylpiperazine [92-54-6]. Similarly, apprx.130 analogs were synthesized.

IT 55117-80-1
RL: BIOL (Biological study)
(condensation of, with (chloropropoxy)dihydrocarbostyril)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



IT 76808-65-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 76808-65-6 CAPLUS
CN 2(1H)-Quinolinone, 7-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propoxy]-3,4-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)

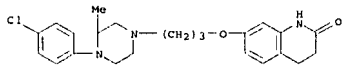


●2 HCl

L9 ANSWER 81 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:425127 CAPLUS
DOCUMENT NUMBER: 95:25127
TITLE: Carbostyril derivatives
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 32 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antihistaminic activity of)
RN 76808-65-6 CAPLUS
CN 2(1H)-Quinolinone, 7-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propoxy]-3,4-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

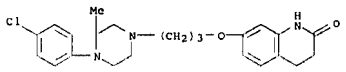
L9 ANSWER 83 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:192375 CAPLUS
DOCUMENT NUMBER: 94:192375
TITLE: 4-Aryl-5-piperazinoalkyl-1,3-dioxol-2-ones, and compositions
INVENTOR(S): Cascio, Giuseppe; Fregnan, Giancarlo; Manghisi, Elso; Porta, Roberto
PATENT ASSIGNEE(S): Istituto Luso Farmaco d'Italia SpA, Italy
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 4235904	A	19801125	US 1979-16135	19790301	<--
AU 7944404	A	19790906	AU 1979-44404	19790220	<--
AU 518565	B2	19811008			
CH 639970	A5	19831215	CH 1979-1825	19790223	<--
FR 2418796	A1	19790928	FR 1979-4928	19790227	<--
FR 2418796	B1	19810724			
ZA 7900922	A	19800227	ZA 1979-922	19790227	<--
CA 1158242	A1	19831206	CA 1979-322408	19790227	<--
NL 7901583	A	19790905	NL 1979-1583	19790228	<--
NL 177404	B	19850416			
NL 177404	C	19850916			
DE 2908148	A1	19790906	DE 1979-2908148	19790302	<--
DE 2908148	C2	19860807			
ES 478696	A1	19800816	ES 1979-478696	19790302	<--
JP 54130569	A	19791009	JP 1979-25004	19790303	<--
JP 62005155	B	19870203			
GB 2017684	A	19791010	GB 1979-7651	19790305	<--
GB 2017684	B	19820818			
PRIORITY APPLN. INFO.:			IT 1978-20841	A 19780303	
			IT 1979-48004	A 19790214	
OTHER SOURCE(S):		MARPAT 94:192375			

JP 55162774	A	19801218	JP 1979-71434	19790606 <--
PRIORITY APPLN. INFO.:			JP 1979-71434	A 19790606
OTHER SOURCE(S):		CASREACT 95:25127		

GI For diagram(s), see printed CA Issue.
AB Forty-seven carbostyrils I [R = H, Q (R6 = H, OH, alkyl, etc.; R4 = H, alkyl; R5 = cycloalkyl, alkanoyl, etc.; p, m = 0-6; r = 2-3); R3 = halo; n = 0-2; R1 = H, alkyl, alkenyl, etc.; R2 = H, alkyl, Ph, Q] were prepared and had antihistaminic and central nervous system depressant activities when tested with guinea pig ileum and in mice, resp. Thus, refluxing 4-methyl-7-[2,3-epoxypropoxy]carbostyril with 4-phenylpiperazine in EtOH 3 h and treating with HCl/EtOH gave 63% 4-methyl-7-[2-hydroxy-(4-phenylpiperazinyl)propoxy]carbostyril-HCl.

IT 76808-65-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 76808-65-6 CAPLUS
CN 2(1H)-Quinolinone, 7-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propoxy]-3,4-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

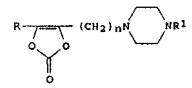
L9 ANSWER 82 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:425121 CAPLUS
DOCUMENT NUMBER: 95:25121
TITLE: Antihistaminic carbostyril derivatives
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
JP 55124766	A	19800926	JP 1979-32486	19790320	<--
JP 63031445	B	19880623			
PRIORITY APPLN. INFO.:			JP 1979-32486	A 19790320	
OTHER SOURCE(S):		CASREACT 95:25121			

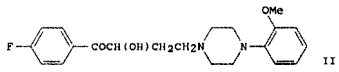
GI For diagram(s), see printed CA Issue.
AB Carbostyrils I [R = H, Q (R3 = H, OH, alkyl, etc.; R4 = H, alkyl; R5 = cycloalkyl, alkanoyl, etc.; l,m = 0-6; r = 2, 3); X = halo; n = 0-2; R1 = H, alkyl, etc.; R2 = H, alkyl, Ph, Q] (131 compds.) were prepared and were tested as antihistaminics in guinea pig ileum. Thus, reaction of 4.4 g 5-(2,3-epoxypropoxy)-3,4-dihydrocarbostyril with 3.4 g 1-phenylpiperazine in MeOH 3 h at 50-60° gave, after treating with HCl, 6.5 g 5-[2-hydroxy-3-(4-phenylpiperazinyl)propoxy]-3,4-dihydrocarbostyril-HCl.

IT 76808-65-6P

GI



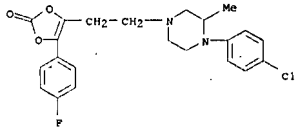
I



II

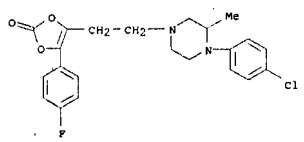
AB Piperazinoalkyldioxolones I (R = optionally substituted Ph, naphthyl; R1 = optionally substituted alkyl, Ph, pyridyl, pyrimidinyl; n = 1-3) were prepared Thus II was treated with COCl2 to give I (R = 4-FC6H4, R1 = 2-MeOC6H4, n = 2) which had an antiulcer ED50 of 30 mg/kg orally in rats. I also have anticholesteremic activity.

IT 71923-05-2P 71923-39-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 71923-05-2 CAPLUS
CN 1,3-Dioxol-2-one, 4-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5-(4-fluorophenyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

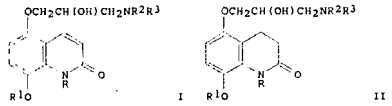
RN 71923-39-2 CAPLUS
CN 1,3-Dioxol-2-one, 4-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 84 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:586412 CAPLUS
DOCUMENT NUMBER: 93:186412
TITLE: Carbostyril compounds
INVENTOR(S): Nakagawa, Kazuyuki; Tominaga, Michiaki; Tone, Hitoshi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: U.S., 15 pp. Cont.-in-part of U.S. Ser. No. 778,537, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4210753	A	19800701	US 1978-965470	19781130 <--
JP 52113979	A	19770924	JP 1976-28957	19760317 <--
JP 59019541	B	19840507		
JP 52136177	A	19771114	JP 1976-52498	19760507 <--
JP 60009501	B	19850311		
ZA 7701461	A	19780830	ZA 1977-1461	19770310 <--
BE 852556	A1	19770718	BE 1977-175856	19770317 <--
PRIORITY APPLN. INFO.:			JP 1976-28957	A 19760317
			JP 1976-52498	A 19760507
			US 1977-778537	A2 19770317

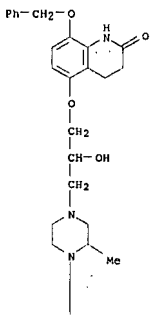
GI



AB 8-Glycidyloxycarbostyrils reacted with amines to give 8-(3-amino-2-hydroxypropoxy)carbostyrils I and II (R = H; R1 = H, phenylalkyl, diphenylalkyl, alkoxyalkyl, hydroxyalkyl, alkanoyl, alkynyl; R2 = H and R3 = pyrrolidinoalkyl, piperazinoalkyl, morpholinoalkyl; or NR2R3 form a piperidino, morpholine, pyrrolidino, or piperazino group), which showed β-adrenergic blocking activity. A mixture of 8-propargyloxy-5-

glycidyloxy-3,4-dihydrocarbostyril, pyrrolidine, and MeOH was kept 12 h at 10-15° to give II (R = H, R1 = propargyl, NR2R3 = pyrrolidino).
IT 65008-48-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and β-adrenergic blocking activity of)
RN 65008-48-2 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-(phenylmethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



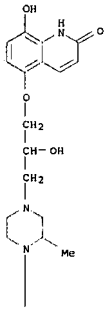
PAGE 2-A

● HCl

IT 65008-50-6P 65034-66-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 65008-50-6 CAPLUS

CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

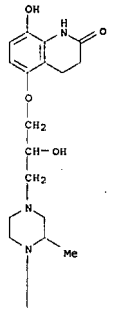


PAGE 2-A

● HCl

RN 65034-66-4 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

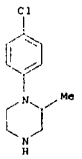
PAGE 1-A



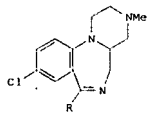
PAGE 2-A

● HCl

IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(ring cleavage of (glycidyloxy)carbostyrils by)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 85 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:542844 CAPLUS
DOCUMENT NUMBER: 93:142844
TITLE: Synthesis and anxiolytic activity of a series of pyrazino[1,2-a][1,4]benzodiazepine derivatives
AUTHOR(S): Smith, R. G.; Lucas, R. A.; Wasley, J. W. F.
CORPORATE SOURCE: Pharm. Div., Ciba-Geigy Corp., Summit, NJ, 07801, USA
SOURCE: Journal of Medicinal Chemistry (1980), 23(8), 952-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 93:142844
GI

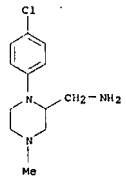


I

AB The synthesis and biol. evaluation of 5 title compds. I (R = Me, Ph, CH2Ph, and 2- or 4-ClC6H4-) and 2 dihydro derivs. for anxiolytic and antidepressant activities are described. I; R = C6H4Cl-2 [74162-29-1] had significant levels of anxiolytic activity but low antidepressant activity.

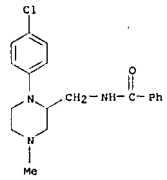
IT 74162-26-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of)

RN 74162-26-8 CAPLUS
CN 2-Piperazinemethanamine, 1-(4-chlorophenyl)-4-methyl- (9CI) (CA INDEX NAME)

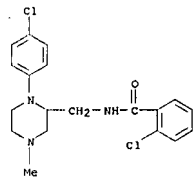


IT 74162-20-2P 74162-21-3P 74162-22-4P
74162-23-5P 74162-24-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

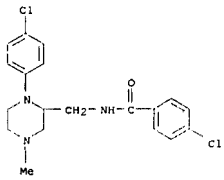
RN 74162-20-2 CAPLUS
CN Benzamide, N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



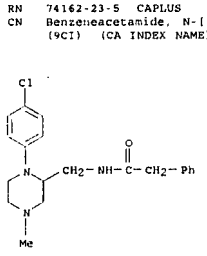
RN 74162-21-3 CAPLUS
CN Benzamide, 2-chloro-N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



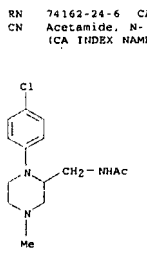
RN 74162-22-4 CAPLUS
CN Benzamide, 4-chloro-N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



RN 74162-23-5 CAPLUS
CN Benzeneacetamide, N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



RN 74162-24-6 CAPLUS
CN Acetamide, N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



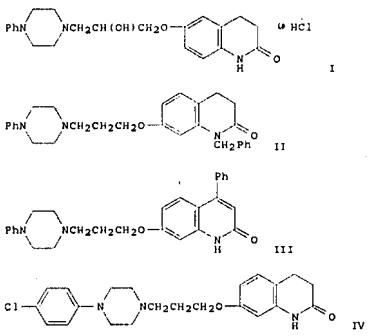
L9 ANSWER 86 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:76316 CAPLUS
DOCUMENT NUMBER: 92:76316
TITLE: Carbostyril derivatives
INVENTOR(S): Banno, Kazuo; Fujioka, Takafumi; Oshiro, Yasuo; Nakagawa, Kazuyuki
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Ger. Offen., 166 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2912105	A1	19791011	DE 1979-2912105	19790327 <--
DE 2912105	C2	19850829		
DE 2912105	C3	19900215		
JP 54130587	A	19791009	JP 1978-37783	19780330 <--
JP 62023750	B	19870525		
CA 1117110	A1	19820126	CA 1979-324227	19790327 <--
DE 2953723	C2	19860710	DE 1979-2953723	19790327 <--
DE 2953723	C3	19890112		
FI 7901034	A	19791001	FI 1979-1034	19790328 <--
FI 70704	B	19860626		
FI 70704	C	19861006		
AU 7945480	A	19791004	AU 1979-45480	19790328 <--
AU 515531	B2	19810409		
US 4734416	A	19880329	US 1979-24602	19790328 <--
BE 875174	A1	19791001	BE 1979-194281	19790329 <--
SE 7902794	A	19791001	SE 1979-2794	19790329 <--
SE 434945	B	19840827		
SE 434945	C	19841220		
NO 7901049	A	19791002	NO 1979-1049	19790329 <--
NO 151321	B	19841210		
NO 151321	C	19850320		
DK 7901286	A	19791026	DK 1979-1286	19790329 <--
DK 158225	B	19900416		
DK 158225	C	19900917		
FR 2421174	A1	19791026	FR 1979-7863	19790329 <--
FR 2421174	B1	19821119		
CH 641455	A5	19840229	CH 1979-2953	19790329 <--
AT 7902351	A	19840415	AT 1979-2351	19790329 <--
AT 376432	B	19841126		
SU 1140687	A3	19850215	SU 1979-2745704	19790329 <--
NL 7902514	A	19791002	NL 1979-2514	19790330 <--
NL 183189	B	19880316		
NL 183189	C	19880816		
GB 2017701	A	19791010	GB 1979-11155	19790330 <--
GB 2017701	B	19830316		
ZA 7901516	A	19800430	ZA 1979-1516	19790330 <--
ES 479134	A1	19800616	ES 1979-479134	19790330 <--
ES 486990	A1	19801001	ES 1979-486990	19791217 <--
ES 486991	A1	19801001	ES 1979-486991	19791217 <--
ES 486992	A1	19801001	ES 1979-486992	19791217 <--
SU 1232144	A3	19860515	SU 1981-3328599	19810908 <--
CH 641350	A5	19840229	CH 1982-1900	19820326 <--

AT 8303915	A	19840415	AT 1983-3915		19831107 <--
AT 376433	B	19841126			
AT 8303916	A	19840415	AT 1983-3916		19831107 <--
AT 376434	B	19841126			
AT 8303917	A	19840415	AT 1983-3917		19831107 <--
AT 376435	B	19841126			
JP 62149664	A	19870703	JP 1986-295668		19861210 <--
JP 63005387	B	19880203			
US 4824840	A	19890425	US 1987-25193		19870312 <--
PRIORITY APPLN. INFO.:			JP 1978-37783	A	19780330
			US 1979-24602	A3	19790328
			AT 1979-2351	A	19790329
			CH 1979-2953	A	19790329

OTHER SOURCE(S): CASREACT 92:76316

GI

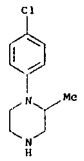


AB Apparatus 160 piperazinoalkoxy- (especially-propoxy)-carbostyrils and/or their 3,4-dihydro derivs. were prepared and tested as antihistaminics, anesthesic- and sedative-enhancers, and analgesics; reference compds. were, e.g., haloperidol, diazepam, or pentabarbitol. Any or all of the piperazine, alkoxy, or carbostyril moieties could be substituted. Thus, the compds. were prepared by treatment of the appropriate hydroxycarbostyril with, a dihalo compound (e.g., Br(CH2)3Cl) or an epoxide, then cyclized via conversion into a bis(haloethyl)amine or treated with a piperazine. Compds. prepared included I-IV.

IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carbostyril derivs.)

RN 55117-80-1 CAPLUS

CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



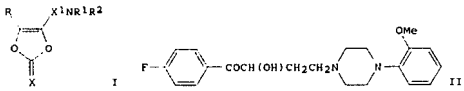
L9 ANSWER 87 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1979:593289 CAPLUS
DOCUMENT NUMBER:	91:193289
TITLE:	4-Aryl-5-aminoalkyl-1,3-dioxol-2-ones and derivatives
PATENT ASSIGNEE(S):	Istituto Luso Farmaco d'Italia S.r.l., Italy
SOURCE:	Belg., 17 pp. CODEN: BEXXAL
DOCUMENT TYPE:	Patent
LANGUAGE:	Dutch
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
BE 874561	A2	19790702	BE 1979-57638	19790302	<--
AU 7944404	A	19790906	AU 1979-44404	19790220	<--
AU 518565	B2	19811008			
CH 639970	A5	19831215	CH 1979-1825	19790223	<--
FR 2418796	A1	19790928	FR 1979-4928	19790227	<--
FR 2418796	B1	19810724			
ZA 7900922	A	19800227	ZA 1979-922	19790227	<--
CA 1158242	A1	19831206	CA 1979-322408	19790227	<--
NL 7901583	A	19790905	NL 1979-1583	19790228	<--
NL 177404	B	19850416			
NL 177404	C	19850916			
DE 2908148	A1	19790906	DE 1979-2908148	19790302	<--
DE 2908148	C2	19860807			
ES 478696	A1	19800816	ES 1979-478696	19790302	<--
JP 54130569	A	19791009	JP 1979-25004	19790303	<--
JP 62005155	B	19870203			
GB 2017684	A	19791010	GB 1979-7651	19790305	<--
GB 2017684	B	19820818			

PRIORITY APPLN. INFO.:	IT 1978-20841	A	19780303	
	IT 1979-48004	A	19790214	

GI

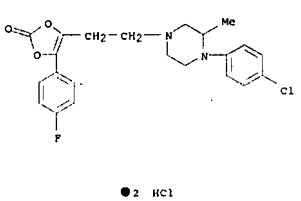


AB Dioxolones I (R = optionally substituted aryl; NR1R2 = secondary amino; X= O, S; X1 = C1-3 alkylene) were prepared Thus, II was treated with COCl2 to give I (R = 4-FC6H4, NR1R2 = 4-(2-methoxyphenyl)piperazino, X = O, X1 = CH2CH2) which had an antiulcer ED30 of 30 mg/kg orally in rats. I also had anticholesteremic activity.

IT 71923-05-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and anticholesteremic and anti-ulcer activity of)

RN 71923-05-2 CAPLUS

CN 1,3-Dioxol-2-one, 4-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5-(4-fluorophenyl)-, dihydrochloride (9CI) (CA INDEX NAME)

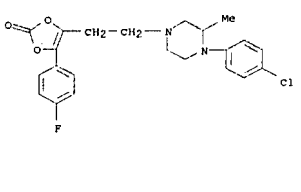


●2 HCl

IT 71923-39-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 71923-39-2 CAPLUS

CN 1,3-Dioxol-2-one, 4-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 88 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1979:137696 CAPLUS
DOCUMENT NUMBER:	90:137696
TITLE:	Carbostyrils
INVENTOR(S):	Tominaga, Michiaki; Tone, Hitoshi; Nakagawa, Kazuyuki
PATENT ASSIGNEE(S):	Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE:	Jpn. Kokai Tokkyo Koho, 6 pp. CODEN: JKXXAF
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
JP 53108989	A	19780922	JP 1977-24042	19770304	<--
JP 59048830	B	19841129			

PRIORITY APPLN. INFO.:	JP 1977-24042	A	19770304	

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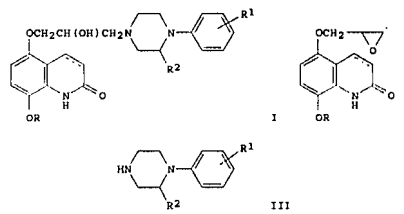


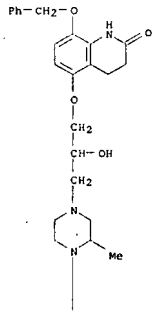
AB Ten carbostyrils I.HCl (R = H, PhCH2; R1 = H, p-MeO or Cl, m-Cl; R2 = H, Me), having β-adrenaline inhibiting activity (no data), were prepared by reaction of II with III. I.HCl (R = H) were also prepared by catalytic reduction of I.HCl (R = PhCH2) over 10% Pd-C. Thus, 2.0 g II (R = PhCH2, 3,4-dihydro) and 2.0 g III (R1 = p-MeO, R2 = H) were stirred in MeOH for 4 h at 40-50° to give 1.2 g I.HCl (R = PhCH2, R1 = p-MeO, R2 = H, 3,4-dihydro).

IT 65008-48-2P 65008-50-6P 65034-66-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 65008-48-2 CAPLUS

CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-(phenylmethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

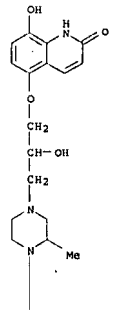


PAGE 2-A

● HCl

RN 65008-50-6 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

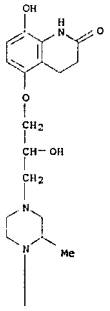


PAGE 2-A

● HCl

RN 65034-66-4 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

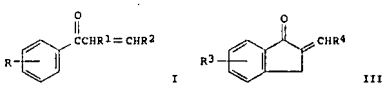


PAGE 2-A

● HCl

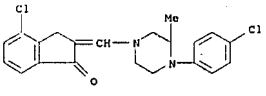
L9 ANSWER 89 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:37465 CAPLUS
DOCUMENT NUMBER: 88:37465
TITLE: 3-Aminoacrylophenones and some related compounds: a new class of anti-inflammatory agents
AUTHOR(S): Gupta, R. C.; Pratap, Ram; Chatterjee, S. K.; Srimal, R. C.; Anand, Nitya
CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1977), 15B(7), 641-4
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 88:37465
GI

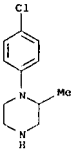


I III

AB Sixteen 3-aminoacrylophenones I (R = 4-F, 2,4-Me2; R1 = H, Me, Et; R2 = piperidino, 4-phenyl-1-piperazinyl, 1-pyrrolidinyl, etc.) (II) were prepared by amination of I (R2 = OH). Similarly 18 2-aminomethylene-1-indanones III (R3 = 4-Cl, 4-, 5-, 6-F; R4 = 4-phenyl-1-piperazinyl, piperidino, etc.) were prepared. Most of II and III have antiinflammatory activity.
IT 65201-34-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 65201-34-5 CAPLUS
CN 1H-Inden-1-one, 4-chloro-2-[[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]methylene]-2,3-dihydro- (9CI) (CA INDEX NAME)



IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with propiophenone)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



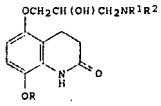
L9 ANSWER 90 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:22663 CAPLUS
DOCUMENT NUMBER: 88:22663

TITLE: Carbostyril derivatives
INVENTOR(S): Tominaga, Michiaki; Tone, Hitochi; Nakagawa, Kazuyuki
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Ger. Offen., 92 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

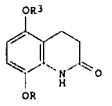
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2711719	A1	19770922	DE 1977-2711719	19770317 <--
DE 2711719	C2	19850214		
JP 52113979	A	19770924	JP 1976-28957	19760317 <--
JP 59019541	B	19840507		
JP 52136177	A	19771114	JP 1976-52498	19760507 <--
JP 60009501	B	19850311		
ZA 7701461	A	19780830	ZA 1977-1461	19770310 <--
CH 619453	A5	19800930	CH 1977-3087	19770311 <--
FI 7700827	A	19770918	FI 1977-827	19770315 <--
FI 63224	B	19830131		
FI 63224	C	19830510		
DK 7701156	A	19770918	DK 1977-1156	19770316 <--
DK 154970	B	19890116		
DK 154970	C	19890612		
SE 7703000	A	19770918	SE 1977-3000	19770316 <--
SE 443140	B	19860217		
SE 443140	C	19860529		
NO 7700940	A	19770920	NO 1977-940	19770316 <--
NO 149388	B	19840102		
NO 149388	C	19840411		
AU 7723299	A	19780928	AU 1977-23299	19770316 <--
AU 513950	B2	19810115		
BE 852556	A1	19770718	BE 1977-175856	19770317 <--
NL 7702896	A	19770920	NL 1977-2896	19770317 <--
NL 179816	B	19860616		
NL 179816	C	19861117		
FR 2344538	A1	19771014	FR 1977-8041	19770317 <--
FR 2344538	B1	19800718		
CA 1081232	A1	19800708	CA 1977-274453	19770317 <--
AT 7701815	A	19810115	AT 1977-1815	19770317 <--
AT 363474	B	19810810		

PRIORITY APPLN. INFO.: JP 1976-28957 A 19760317
JP 1976-52498 A 19760507

OTHER SOURCE(S): MARPAT 88:22663
GI



I



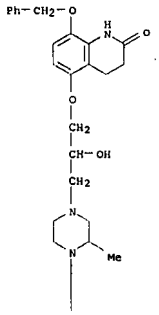
II

AB Carbostyril derivs. (.apprx.130 compds.), including I [R = H, CH2CH2OMe, allyl, propargyl, CH2Ac, Bu, CH2CH2OH, CH2CO2H, CH2CONH2, Me, CH2Ph, CH2C6H4Ac-4, cyclohexylcarbonyl, CH2CO2Et; R1 = H, R2 = CH2CH2C6H3(OMe)2-3,4, allyl, CMe3, CHPh2, morpholinopropyl, CMe2CH2Ph, CH2CHPh2, CHMe2; NR1R2 = 3-methyl-4-phenylpiperazino] were prepared Thus, II (R = R3 = H) was treated with HC.tplbond.CCH2Br, II (R = CH2C.tplbond.CH, R3 = H) treated with epichlorohydrin, II (R = CH2C.tplbond.CH, R3 = 2,3-epoxypropyl) treated with Me3CNH2 to give I (R = CH2C.tplbond.CH, R1 = H, R2 = CMe3), which at 300 mg/kg i.v. gave 100% inhibition of isoprenalin-induced increase in heart rate in dogs.

IT 65008-48-2P 65008-50-6P 65034-66-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 65008-48-2 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-(phenylmethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

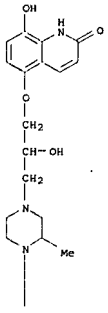


PAGE 2-A

● HCl

RN 65008-50-6 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

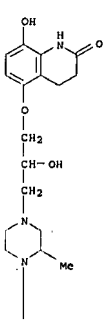


PAGE 2-A

● HCl

RN 65034-66-4 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

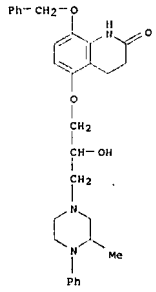
PAGE 1-A



PAGE 2-A

● HCl

IT 65023-17-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sympatholytic activity of)
RN 65023-17-8 CAPLUS
CN 2(1H)-Quinolinone, 3,4-dihydro-5-[2-hydroxy-3-(3-methyl-4-phenyl-1-piperazinyl)propoxy]-8-(phenylmethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)



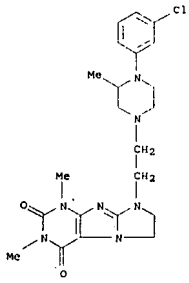
● HCl

L9 ANSWER 91 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:592771 CAPLUS
DOCUMENT NUMBER: 85:192771
TITLE: 8-Aminotheophylline derivatives
INVENTOR(S): Quelet, Jean R.
PATENT ASSIGNEE(S): Laboratoire le Brun S. A., Fr.
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German

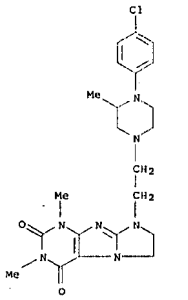
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2609397	A1	19760923	DE 1976-2609397	19760306 <--
FR 2303551	A1	19761008	FR 1975-7675	19750312 <--
ZA 7601234	A	19770223	ZA 1976-1234	19760302 <--
GB 1536492	A	19781220	GB 1976-8487	19760303 <--
JP 51113898	A	19761007	JP 1976-24723	19760309 <--
ES 445944	A1	19770516	ES 1976-445944	19760310 <--
BE 839419	A1	19760913	BE 1976-165037	19760311 <--
CH 597231	A5	19780331	CH 1976-3060	19760311 <--
AU 7611975	A	19770915	AU 1976-11975	19760312 <--
AU 501358	B2	19790621		

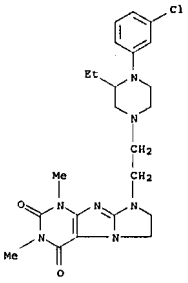
PRIORITY APPLN. INFO.: FR 1975-7675 A 19750312
OTHER SOURCE(S): MARPAT 85:192771
GI For diagram(s), see printed CA Issue.
AB Purinediones [I; R = H, Me, Et, 3-MeOC6H4; R1n = e.g., H, 3-Cl, 3-Br, 3-F, 3,4-Cl2, 3,4-Me2; n = 2, 3, 4; m = 2, 3, 6; (CH2)m = CH2CHMe], with antitussive, antihistaminic, analgesic, inflammation-inhibiting, tranquilizing, and sedative activities, are prepared by reaction of 9-(chloroalkyl)tetrahydropyrimidopurinediones with phenylpiperazines. The pyrimidopurinediones are obtained by condensation of 8-chloro-7-(chloroalkyl)theophyllines with amino alcs. and replacement of the OH with Cl. Thus, reaction of 5.75 g 9-(2-chloroethyl)-6,7,8,9-tetrahydro-1,3-dimethylpyrimido[2,1-f]purine-2,4(1H,3H)-dione with 7.5 g 1-(3-chlorophenyl)piperazine 2 hr at 180-90° gives 4.7 g I (R = H, R1 = 3-Cl, m = 2, n = 3).
IT 60987-61-3P 60987-62-4P 60987-63-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and pharmacol. activity of)
RN 60987-61-3 CAPLUS
CN 1H-Imidazo[2,1-f]purine-2,4(3H,6H)-dione, 8-[2-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-7,8-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 60987-62-4 CAPLUS
CN 1H-Imidazo[2,1-f]purine-2,4(3H,6H)-dione, 8-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-7,8-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



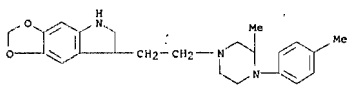
RN 60987-63-5 CAPLUS
CN 1H-Imidazo[2,1-f]purine-2,4(3H,6H)-dione, 8-[2-[4-(3-chlorophenyl)-3-ethyl-1-piperazinyl]ethyl]-7,8-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



L9 ANSWER 92 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:17426 CAPLUS
DOCUMENT NUMBER: 84:17426
TITLE: Aminoalkyleneindolines
INVENTOR(S): Allen, George R., Jr.; Littell, Ruddy
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Can., 14 pp.
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

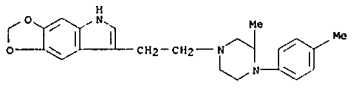
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 972372	A1	19750805	CA 1972-142893	19720524 <--

PRIORITY APPLN. INFO.: US 1972-242734 A 19720410
GI For diagram(s), see printed CA Issue.
AB The title compds. I (R = R1 = MeO; RR1 = OCH2O; R = MeO, R1 = H; R2 = H, Me; R3 = H, Me; R4 = H, 2-MeO, 4-Me, 2-Cl), which reduced motor activity in mice 50% at 0.2-25 mg/ml, were prepared by reduction of the corresponding indoles by hydrogenation in HCl or by Sn-HCl.
IT 49632-90-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 49632-90-8 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

IT 40119-10-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)
RN 40119-10-6 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 93 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:443207 CAPLUS
DOCUMENT NUMBER: 83:43207
TITLE: 2-(Piperazinylalkyl)isoquinolinediones
INVENTOR(S): Kutter, Eberhard; Austel, Volkhard; Eberlien, Wolfgang; Heider, Joachim
PATENT ASSIGNEE(S): thomae, Fed. Rep. Ger.
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

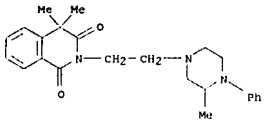
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 2345422	A1	19750320	DE 1973-2345422	19730908	<--
DE 2345422	C2	19831222			
AT 7406514	A	19751015	AT 1974-6514	19740808	<--
AT 330777	B	19760726			
FI 7402465	A	19750309	FI 1974-2465	19740821	<--
FI 52219	B	19770331			
ES 429473	A1	19760901	ES 1974-429473	19740823	<--
US 3948898	A	19760406	US 1974-503072	19740904	<--
SU 528035	A3	19760905	SU 1974-2057995	19740904	<--
AU 7473023	A	19760311	AU 1974-73023	19740905	<--
BE 819651	A1	19750306	BE 1974-148302	19740906	<--
SE 7411312	A	19750310	SE 1974-11312	19740906	<--
SE 424863	B	19820816			

SE 424863	C	19821125			
NL 7411843	A	19750311	NL 1974-11843	19740906	<--
NL 176363	B	19841101			
NL 176363	C	19850401			
NO 7403220	A	19750311	NO 1974-3220	19740906	<--
NO 140978	B	19790910			
FR 2242979	A1	19750404	FR 1974-30387	19740906	<--
DK 7404727	A	19750505	DK 1974-4727	19740906	<--
JP 50050381	A	19750506	JP 1974-102862	19740906	<--
JP 59006868	B	19840215			
DD 115122	A5	19750912	DD 1974-180966	19740906	<--
HU 167869	B	19751225	HU 1974-TO980	19740906	<--
ZA 7405688	A	19760526	ZA 1974-5688	19740906	<--
GB 1446791	A	19760818	GB 1974-39083	19740906	<--
CH 605778	A5	19781013	CH 1974-12189	19740906	<--
CH 605779	A5	19781013	CH 1977-16014	19740906	<--
RO 63655	A1	19781015	RO 1974-79932	19740906	<--
CS 185660	B2	19781031	CS 1974-6150	19740906	<--
PL 91712	B1	19770331	PL 1974-173958	19740907	<--
ES 433958	A1	19761116	ES 1975-433958	19750120	<--
ES 433959	A1	19761116	ES 1975-433959	19750120	<--
SU 538664	A3	19761205	SU 1975-2145942	19750620	<--
SU 545256	A3	19770130	SU 1975-2145935	19750620	<--
AT 7505606	A	19760515	AT 1975-5606	19750721	<--
AT 334174	B	19760110			
AT 7505607	A	19760515	AT 1975-5607	19750721	<--
AT 334375	B	19760110			
US 4021558	A	19770503	US 1976-651568	19760122	<--

PRIORITY APPLN. INFO.:

DE 1973-2345422	A	19730908
DE 1973-2345423	A	19730908
AT 1974-6514	A	19740808
US 1974-503072	A2	19740904

GI For diagram(s), see printed CA Issue.
AB Twenty-five isoquinolinediones I (R = Ph, substituted Ph, or 2-pyridyl; R1 = H or Me; R2 = H, F, Cl, or MeO; n = 2 or 3), useful as antihypertensives or sedatives or in tachycardia treatment (no data), were prepared by reaction of the isochromandiones (II, X = O) or isoquinolinediones II (X = NH) with (1-piperazinyl)alkylamines or (1-piperazinyl)alkyl chlorides, resp., or by reaction of the isoquinolinediones (II, X = N(CH2)nCl] with the piperazines.
IT 55974-45-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of antihypertensive and sedative)
RN 55974-45-3 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-[3-methyl-4-phenyl-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with isoquinolinediones)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 94 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:171026 CAPLUS
DOCUMENT NUMBER: 82:171026
TITLE: 1,3-Dialkyl-4-aminouracils
INVENTOR(S): Hartleben, York; Goering, Joachim; Tauscher, Manfred; Rohte, Oskar; Brenner, Guenter; Firma Johann A. Wuelfing
SOURCE: Ger. Offen., 25 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

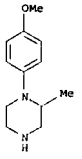
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 2329399	A1	19750102	DE 1973-2329399	19730608	<--
FI 7401579	A	19741209	FI 1974-1579	19740523	<--
AT 7404300	A	19760115	AT 1974-4300	19740524	<--
AT 332425	B	19760927			
JP 50052077	A	19750509	JP 1974-62447	19740601	<--
SE 7407471	A	19741209	SE 1974-7471	19740606	<--
NL 7407611	A	19741210	NL 1974-7611	19740606	<--
BE 816055	A1	19740930	BE 1974-145190	19740607	<--
FR 2232320	A1	19750103	FR 1974-19693	19740607	<--
HU 168153	B	19760228	HU 1974-WU16	19740607	<--
DD 119233	A5	19760412	DD 1974-179053	19740610	<--

PRIORITY APPLN. INFO.:

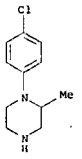
DE 1973-2329399	A	19730608

GI For diagram(s), see printed CA Issue.

AB About 40 uracils I and II [R = Me, Me2CH, or Bu; R1 = CH2CH2OH, CH2CH2SO2C6H4Me-4, or (CH2)3OH; R2 = Me, Pr, CH2CHMeOH, CH2Ph, (CH2)3NH2, CO2Et, C6H4COMe-4 or -2, 2-pyridyl, CHPhC6H4Cl-4, etc.; R3 = H or Me] were prepared by reaction of 4-chlorouracils with amines. I and II had anticholesteremic, choleretic, and diuretic activity when tested orally in the rat. LD50 values were obtained in the mouse. Thus, 1,3-dibutyl-4-chlorouracil and H2NCH2CH2OH were refluxed in EtOH to give 97% I (R = Bu, R1 = CH2CH2OH).
IT 35947-12-7 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with chlorouracils)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

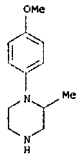


RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)

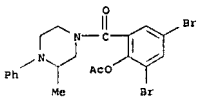


L9 ANSWER 95 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:170836 CAPLUS
DOCUMENT NUMBER: 82:170836
TITLE: Synthesis of new piperazine derivatives. 1-Alkyl(or aroyl)-4-(N-alkyl(or aroyl) piperazinyl)-1-butene-3-ones
AUTHOR(S): Baboulene, Michel; Sturtz, Georges
CORPORATE SOURCE: Lab. Chim. Hetero-Org., U.E.R. Sci., Brest, Fr.
SOURCE: Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques (1975), 280(3), 149-51

CODEN: CHDCAQ; ISSN: 0567-6541
DOCUMENT TYPE: Journal
LANGUAGE: French
OTHER SOURCE(S): CASREACT 82:170836
GI For diagram(s), see printed CA Issue.
AB Piperazines I(R=Me, Ph, 4-FC6H4, 4-MeOC3H4, Ch2Ph; R1=CHMe2, Ph, 4-BrC6H4, 4-FC6H4, 4-MeC6H4) were prepared in 25-45% yield by treating the phosphonates II with RICHO. II were prepared in .apprx.95% yield by treating (EtO)2P(O)CH2CBr:CHBr with Et2NH, hydrolyzing (EtO)2P(O)CH:C(NEt2)CH2Br, and treating (EtO)2P(O)CH2COCH2Br with the piperazine derivs. Ketones did not react with II.
IT 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bromo(oxo)alkylphosphonate)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 96 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1974:552164 CAPLUS
DOCUMENT NUMBER: 81:152164
TITLE: Possible anti-Parkinsonian compounds. II. Synthesis of 3,5-dihalo acetyl salicyloylamines, piperazines, and phenothiazines
AUTHOR(S): Tiwari, S. S.; Pandey, V. K.
CORPORATE SOURCE: Dep. Chem., Lucknow Univ., Luchnow, India
SOURCE: Journal of the Indian Chemical Society (1973), 50(12), 800-1
CODEN: JICSAH; ISSN: 0019-4522
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Dihaloacetylsalicylamides I (R = Cl, Br; R1 = R2 = Me, Et, Ph, CH2CH2OH; NR1R2 = morpholino, piperidino, pyrrolidino, phenothiazino, N-arylpiperazino) were prepared by acylating the dihalosalicylic acids, chlorinating, and treating with the amine.
IT 54295-55-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 54295-55-5 CAPLUS
CN Piperazine, 4-[2-(acetyloxy)-3,5-dibromobenzoyl]-2-methyl-1-phenyl- (9CI) (CA INDEX NAME)



IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with acetyldihalosalicoyl chlorides)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

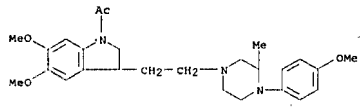
L9 ANSWER 97 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1974:141107 CAPLUS
DOCUMENT NUMBER: 80:141107
TITLE: Pharmacological analysis of the role of the nervous system in inflammation
AUTHOR(S): Trinus, F. P.
CORPORATE SOURCE: Kiev, USSR
SOURCE: Farmakologiya i Toksikologiya (Kiev) (1973), No. 8, 40-7
CODEN: FATOBP; ISSN: 0430-0939
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Seven compds. which affect the central nervous system and 17 compds. which affect the autonomic nervous system were tested for their antiinflammatory effects in rats with formalin induced inflammation. Compds. which inhibit the central nervous system, such as chloral hydrate [302-17-0], hexenal [50-09-9], aminazine [50-53-3], and reserpine [50-55-5], were antiinflammatory, whereas central nervous system stimulators were not. The ganglion stimulator, dimethylphenylpiperazine [33905-48-5], had a short-acting antiinflammatory effect, whereas gangliolytics did not. The cholinomimetic, carbachol [51-83-2], the anticholinesterases, eserine [57-47-6] and proserine [114-80-7], the sympathomimetics, adrenaline [51-43-4], octadine [60-02-6], the α-adrenolytics, dihydroergotoxin [11032-41-0] and phentolamine [50-60-2], and the monoamine oxidase inhibitors ipraxide [54-92-2], malamide [4387-09-1], and transamine [3721-28-6] were also antiinflammatory.

L9 ANSWER 98 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:492287 CAPLUS
DOCUMENT NUMBER: 79:92287
TITLE: 1-Acyl-3-(2-[4-phenyl-1-piperazinyl]ethyl]indolines
INVENTOR(S): Allen, George Rodger, Jr.; McEvoy, Francis J.; De Vries, Vern G.; Moran, Daniel B.; Littell, Ruddy
PATENT ASSIGNEE(S): American Cyanamid Co.
SOURCE: U.S., 14 pp.

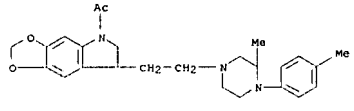
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 3751417	A	19730807	US 1971-171319		19710812 <--
PRIORITY APPLN. INFO.:			US 1971-171319	A	19710812

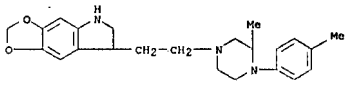
GI For diagram(s), see printed CA Issue.
AB Preparation of the title indoline deriva. with analgesic properties is described. In an example, 1-acetyl-3-indolineacetic acid (I) was reduced (borane/THF) to the alc. II which on treatment with PBr3 gave III. III on reaction with 1-phenylpiperazine gave IV (R1 = R2 = R3 = H, R4 = Ac). Also reported are IV [R1 = 5,6-(MeO)2, 5,6-methylenedioxy; R2 = H, Me; R3 = H, MeO; R4 = Bz, p-ClC6H4CO, p-O2NC6H4CO, EtCO, Ac, PrCO].
IT 40118-64-7P 40118-66-9P 49632-90-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 40118-64-7 CAPLUS
CN 1H-Indole, 1-acetyl-2,3-dihydro-5,6-dimethoxy-3-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 40118-66-9 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 5-acetyl-6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

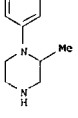


RN 49632-90-8 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]-, trihydrochloride (9CI) (CA INDEX NAME)

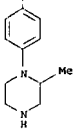


●3 HCl

IT 35947-11-6 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (bromoethyl)indolines)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



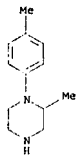
L9 ANSWER 99 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:417847 CAPLUS
DOCUMENT NUMBER: 79:17847
TITLE: Thermodynamics of the complexing of silver by piperazine and some of its derivatives in water-ethanol solution

AUTHOR(S): Enea, O.; Houngbossa, K.; Berthon, G.
CORPORATE SOURCE: Lab. Thermodyn. Chim. Electrochim., Univ. Poitiers, Poitiers, Fr.
SOURCE: Thermochimica Acta (1973), 6(3), 309-17
CODEN: THACAS; ISSN: 0040-6031
DOCUMENT TYPE: Journal
LANGUAGE: French

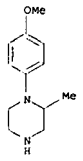
AB The stability consts. of the complexes of Ag+ ion with piperazine and its 2-methyl-, 2-methyl-1-m-tolyl-, 2-methyl-1-p-tolyl-, and 1-(p-methoxyphenyl)-2-methyl- derivs. are obtained at 25° in water-EtOH (52%, w/w) and KNO3 0.1 M ionic strength, by means of corresponding metal-complex electrodes. The enthalpies of formation are determined by direct calorimetry. The thermodn. functions ΔGn°, ΔHn°, ΔSn° are discussed in relation to the ability of each amine to coordinate, in terms of the nature and position of the entering group.

IT 35947-11-6 35947-12-7
RL: PROC (Process)
(complex formation of, with silver ion, stability of)

RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 100 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:84255 CAPLUS
DOCUMENT NUMBER: 78:84255

TITLE: 3-[2-(4-Phenyl-1-piperazinyl)ethyl]indolines
INVENTOR(S): Allen, George Rodger, Jr.; McEvoy, Francis Joseph; DeVries, Vern Gordon; Moran, Daiel Bryan; Litell, Ruddy
PATENT ASSIGNEE(S): American Cyanamid Co.
SOURCE: Ger. Offen., 87 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 2225765	A	19721207	DE 1972-2225765	19720526	<--
US 3751416	A	19730807	US 1971-147700	19710527	<--
ZA 7202916	A	19730228	ZA 1972-2916	19720501	<--
CA 1014154	A1	19770719	CA 1972-140989	19720501	<--
GB 1382916	A	19750205	GB 1972-20674	19720503	<--
GB 1382917	A	19750205	GB 1973-56237	19720503	<--
AU 7241918	A	19731108	AU 1972-41918	19720504	<--
CS 185203	B2	19780915	CS 1972-3454	19720519	<--
CS 185244	B2	19780915	CS 1976-248	19720519	<--
CS 185245	B2	19780915	CS 1976-251	19720519	<--
PL 81987	B1	19751031	PL 1972-155596	19720525	<--
PL 92627	B1	19770430	PL 1972-176212	19720525	<--
PL 92635	B1	19770430	PL 1972-176213	19720525	<--
PL 92634	B1	19770430	PL 1972-176214	19720525	<--
BE 784012	A1	19721127	BE 1972-117944	19720526	<--
NL 7207129	A	19721129	NL 1972-7129	19720526	<--
FR 2139158	A1	19730105	FR 1972-18968	19720526	<--
DD 100471	A5	19730920	DD 1972-163237	19720526	<--
SU 489321	A3	19751025	SU 1972-1792254	19720526	<--
SU 489322	A3	19751025	SU 1972-1960739	19720526	<--
CH 579563	A5	19760915	CH 1972-7843	19720526	<--
RO 60145	A1	19760915	RO 1972-71032	19720526	<--
CH 582142	A5	19761130	CH 1976-7597	19720526	<--
CH 582172	A5	19761130	CH 1976-7598	19720526	<--
CH 583700	A5	19770114	CH 1976-7595	19720526	<--
CH 583701	A5	19770114	CH 1976-7596	19720526	<--
NO 136795	B	19770801	NO 1972-1869	19720526	<--
SE 395455	B	19770815	SE 1972-6918	19720526	<--
SE 397524	B	19771107	SE 1974-2374	19720526	<--
SE 397525	B	19771107	SE 1974-2375	19720526	<--
RO 63715	A1	19781015	RO 1972-80196	19720526	<--
RO 63730	A1	19781115	RO 1972-80194	19720526	<--
RO 64489	A1	19790515	RO 1972-80193	19720526	<--
HU 166178	B	19750228	HU 1972-AE360	19720527	<--
HU 167203	B	19750927	HU 1972-AE400	19720527	<--
HU 168720	B	19760728	HU 1972-AE401	19720527	<--
ES 409281	A1	19760316	ES 1972-409281	19721204	<--
ES 409282	A1	19760316	ES 1972-409282	19721204	<--
ES 409283	A1	19760316	ES 1972-409283	19721204	<--
ES 409284	A1	19760316	ES 1972-409284	19721204	<--
US 3900495	A	19750819	US 1973-350445	19730412	<--
SU 575024	A3	19770930	SU 1973-1953507	19730726	<--
SU 488408	A3	19751015	SU 1973-1960738	19730913	<--
SE 7600531	A	19760120	SE 1976-531	19760120	<--
CA 1056821	A2	19790619	CA 1977-276961	19770426	<--

PRIORITY APPLN. INFO.:

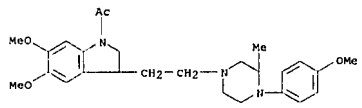
US 1971-147700	A	19710527
CA 1972-140989	A3	19720501
ES 1972-403245	A3	19720527

GI For diagram(s), see printed CA Issue.

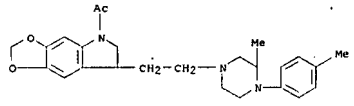
AB Approx. 60 piperazinylethylindolines I (R = Ac, Bz, H, etc.; R1 = Me, H; R2 = H, o-, p-MeO, o-, m-Me, o-, m-Cl, etc.; R3 = H, MeO, Br, O2N, Ac, etc.; R4 = MeO), tranquilizers, were prepared by reaction of a piperazine with a 3-(2-bromoethyl)indoline. Dosages of I for 50% reduction of motor activity in mice were given.

IT 40118-64-7P 40118-66-9P 40118-85-2P
40119-01-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

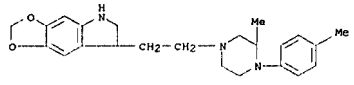
RN 40118-64-7 CAPLUS
CN 1H-Indole, 1-acetyl-2,3-dihydro-5,6-dimethoxy-3-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



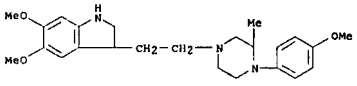
RN 40118-66-9 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 5-acetyl-6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 40118-85-2 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

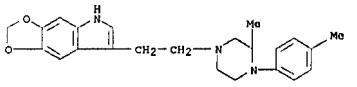


RN 40119-01-5 CAPLUS
CN 1H-Indole, 2,3-dihydro-5,6-dimethoxy-3-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



IT 40119-10-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)

RN 40119-10-6 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

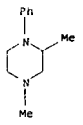


L9 ANSWER 101 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:405077 CAPLUS
DOCUMENT NUMBER: 77:5077
TITLE: Syntheses of heterocyclic compounds. CDLX. Benzyne reaction. XIII. Benzyne reaction of halogenobenzenes with N-alkylmorpholines
AUTHOR(S): Kametani, T.; Kigasawa, K.; Hiiragi, M.; Aoyama, T.
CORPORATE SOURCE: Pharm. Inst., Tohoku Univ., Sendai, Japan
SOURCE: Journal of Organic Chemistry (1972), 37(9), 1450-3
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 77:5077

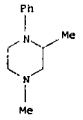
AB The benzyne reaction of N-alkylmorpholines with bromobenzene in the presence of NaNH2 gives mixts. of N-alkylanilines and N-alkyl-N-β-hydroxyethylanilines. Minor amts. of ylide rearrangement products were obtained with other tertiary amines.

IT 33905-48-5P 33905-49-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 33905-48-5 CAPLUS
CN Piperazine, 2,4-dimethyl-1-phenyl- (9CI) (CA INDEX NAME)



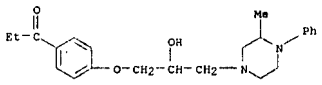
RN 33905-49-6 CAPLUS
CN Piperazine, 2,4-dimethyl-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



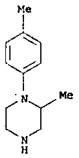
● HCl

L9 ANSWER 102 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:149138 CAPLUS
DOCUMENT NUMBER: 76:149138
TITLE: Agents acting on the central nervous system. 14. 1-(p-alkanoylphenoxy)-3-(N4-arylpiperazinyl)propan-2-ols. New class of antidepressants
AUTHOR(S): Rastogi, S. Nivas; Anand, Nitya; Prasad, C. R.
CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, India
SOURCE: Journal of Medicinal Chemistry (1972), 15(3), 286-91
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 76:149138
AB 1-(P-alkanoylphenoxy)-3-(4-piperazinyl)-2-propanols (I), 1,3-bis(aryloxy)-2-propanols (II) and related compds. were prepared, e.g., by condensation of 1-aryloxy-2,3-epoxypropanes with amines and screened pharmacol. 1-(P-propionylphenoxy)-3-(4-phenylpiperazinyl)-2-propanol (III) [34675-77-9] counteracted reserpine-induced depression in cats and potentiated amphetamine-induced stimulation in mice and rats at 5-10 mg/kg; at 100 mg/kg, III counteracted amphetamine-induced hyperactivity and toxicity in aggregated mice. Structural modifications of II gave decreased antidepressant activity, thus III activity is specific and very similar to that of amitriptyline [50-48-6] and imipramine [50-49-7].
IT 36119-92-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmacology of)

RN 36115-92-1 CAPLUS
CN 1-Propanone, 1-[4-[2-hydroxy-3-(3-methyl-4-phenyl-1-piperazinyl)propoxy]phenyl]- (9CI) (CA INDEX NAME)

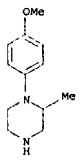


L9 ANSWER 103 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:90929 CAPLUS
DOCUMENT NUMBER: 76:90929
TITLE: Heats of protonation of piperazine and some derivatives in water-ethanol media
AUTHOR(S): Berthon, Guy; Enea, Octav; Houngbossa, Kouassi
CORPORATE SOURCE: Lab. Thermodyn. Chim. Electrochim., Univ. Poitiers, Poitiers, Fr.
SOURCE: Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques (1971), 273(18), 1140-3
CODEN: CHDCAQ; ISSN: 0567-6541
DOCUMENT TYPE: Journal
LANGUAGE: French
AB At 25° with water-52% EtOH as solvent and ionic strength 0.1 mole/dm3 (KNO3), the standard Gibbs free energies (in kcal/mole), standard enthalpies (in kcal/mole), and standard entropies (in cal/degree mole), resp., for the protonation reactions AHn-1(n-1)+ + H+ ↔ AHn+ (n = 1,2) are: piperazine -12.60, -10.5, +7.0 for n = 1, -7.10, -7.0, 0 for n = 2; 2-methylpiperazine -12.22, -10.4, +6.1 for n = 1, -6.98, -6.4, +1.9 for n = 2; 2-methyl-1-m-tolylpiperazine -11.12, -8.8, +7.8 for n = 1; 2-methyl-1-p-tolylpiperazine -11.17, -8.1, +10.0 for n = 1; 1-(p-methoxyphenyl)-2-methylpiperazine -11.23, -8.4, +9.5 for n = 1.
IT 35947-11-6 35947-12-7
RL: PROC (Process) (thermodynamics of protonation of)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



RN 35947-12-7 CAPLUS

CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

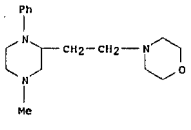


L9 ANSWER 104 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:72551 CAPLUS
DOCUMENT NUMBER: 76:72551
TITLE: 5-(2-Aminoethyl)-2,3-piperazinediones and 3-(2-aminoethyl)piperazines
INVENTOR(S): Lunsford, Carl D.; Cale, Albert D., Jr.
PATENT ASSIGNEE(S): A. H. Robins Co., Inc.
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

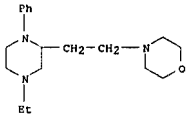
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2120367	A	19711111	DE 1971-2120367	19710426 <--
ES 389548	A1	19730616	ES 1971-389548	19710325 <--
GB 1340894	A	19731219	GB 1971-10219	19710420 <--
FR 2092096	A1	19720121	FR 1971-14802	19710426 <--
FR 2092096	A5	19720121		
ZA 7102663	A	19720126	ZA 1971-2663	19710426 <--
CH 534685	A	19730430	CH 1971-6092	19710426 <--
US 3862938	A	19750128	US 1972-230459	19720229 <--
PRIORITY APPLN. INFO.:			US 1970-32346 A	19700427

GI For diagram(s), see printed CA Issue.
AB Title compds., useful as antiviral agents against myxoviruses, were prepared by reaction of 5-(2-chloroethyl)-2,3-piperazinediones with amines to give the corresponding aminoethylpiperazinediones (I) and reduction of I with LiAlH4 to give the piperazines (II). Thus, I (R = Me, R1 = Cl) was refluxed 4 hr in morpholine to give 70 I (R = Me, R1 = morpholino) (III). Similarly prepared were 7 addnl. I, e.g. (R and R1 given): iso-Pr, morpholino (IV); iso-Pr, NMe2 (V); cyclohexyl, morpholino (VI); cyclohexyl, NMe2 (VII). III was refluxed 4 hr with LiAlH4 in THF to give 60% II (R = Me, R1 = morpholino). Similarly prepared were II (R and R1 given): Et, morpholino; cyclohexyl, morpholino (VIII); cyclohexyl, NMe2. IV, VII, and VIII were active against influenza, V, VI, and VII against parainfluenza type III, and VII was active against respiratory syncytial virus.
IT 34933-34-1P 34933-35-2P 34933-38-5P
RL: SPN (Synthetic preparation); PREP (Preparation)

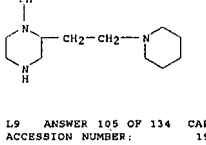
(preparation of)
RN 34933-34-1 CAPLUS
CN Morpholine, 4-[2-(4-methyl-1-phenyl-2-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 34933-35-2 CAPLUS
CN Morpholine, 4-[2-(4-ethyl-1-phenyl-2-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

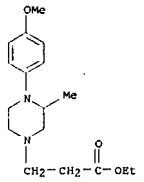


RN 34933-38-5 CAPLUS
CN Piperazine, 1-phenyl-2-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



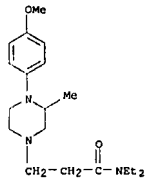
L9 ANSWER 105 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:139148 CAPLUS
DOCUMENT NUMBER: 74:139148
TITLE: Effects of morpholino-, pyrrolidino-, piperazino-, and cyclooctyl-derivatives of β-alanine on brain amines and amino acids
AUTHOR(S): Leonard, Brian E.; Liska, Kenneth J.
CORPORATE SOURCE: Imp. Chem. Ind. Ltd., Cheshire, UK
SOURCE: Life Sciences (1971), 10(2)(Pt. 1), 93-104
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

GI For diagram(s), see printed CA Issue.
AB Eight β-alanine derivs., related structurally to the D-ring of lysergic acid diethylamide (LSD), were synthesized and examined for psychotomimetic activity in rats. On the basis of 11 parameters studied, such as behavioral effects, hyperthermia, and effects on brain catechol amines, little similarity was observed between these derivs. and LSD. Et 3-(cyclooctylamino)propionate (I) exhibited the action profile most like LSD, followed by 3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]-N,N-diethylpropionamide (II), Et 3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propionate (III), and 3-(2-(1-pyrrolidinyl)ethylamino)-N,N-diethylpropionamide. 3-(2-Mor-pholinoethylamino)-N,N-diethylpropionamide showed no neurochem. effects similar to LSD.
IT 32559-61-8 32835-69-1
RL: BIOL (Biological study)
(brain amino acids and pyrocatechol amines in response to)
RN 32559-61-8 CAPLUS
CN 1-Piperazinepropanoic acid, 4-(4-methoxyphenyl)-3-methyl-, ethyl ester, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 32835-69-1 CAPLUS
CN 1-Piperazinepropanamide, N,N-diethyl-4-(4-methoxyphenyl)-3-methyl-, hydrochloride (9CI) (CA INDEX NAME)

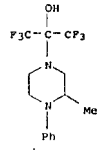


●x HCl

L9 ANSWER 106 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:78383 CAPLUS
DOCUMENT NUMBER: 72:78383
TITLE: Herbicidal halogen-contnining amino alcohols
PATENT ASSIGNEE(S): Esso Research and Engineering Co.
SOURCE: Brit., 19 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1178420		19700121	GB 1967-46007	19671009 <--
DE 1643315			DE	
US 3520929		19700721	US	19661019 <--
PRIORITY APPLN. INFO.:			US	19661019

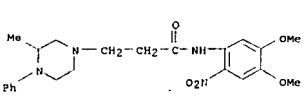
AB Herbicidal and fungicidal title compds. were prepared by reaction of halo ketones and aldehydes with amines. Thus 83 g (F3C)2O was passed into a solution of 60 g N,N-dimethyl-1,3-propanediamine in 200 ml Et2O at -50° to give 2-[3-(dimethylamino)propylamino]-1,1,1,3,3,3-hexafluoro-2-propanol, m. 62.5-3.5°. Similarly 58 compds. were prepared, and screened as pre- and postemergent herbicides at 10 lbs/acre on millet, ryegrass, sorghum, aster, buckwheat, and turnip. Bean rust fungus Uromyces phaseoli and Erysiphe polygoni bean mildew were controlled by 1000 ppm of most of the compds. tested.
IT 26799-46-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 26799-46-2 CAPLUS
CN 1-Piperazinemethanol, 3-methyl-4-phenyl-α,α-bis(trifluoromethyl)- (8CI) (CA INDEX NAME)



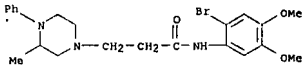
L9 ANSWER 107 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:66985 CAPLUS
DOCUMENT NUMBER: 72:66985
TITLE: Piperazinyl derivatives
PATENT ASSIGNEE(S): Byk-Gulden Lomberg Chemische Fabrik G.m.b.H.
SOURCE: Brit., 9 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1166595		19691008	GB 1968-8503	19680221 <--
DE 1670200			DE	
FR 1577338			FR	
PRIORITY APPLN. INFO.:			DE	19670322

AB Piperazinylpropionic acid anilides, useful for sedative, neuroleptic, and analgesic properties, are prepared Thus, a hot solution of 10 g 4-(β-bromopropionylamino)-5-nitroveratrole (preparation of this and similar compds. given) in 50 ml MeCN is slowly poured into a solution of 6 g ethyldicyclohexylamine and 5.1 g 1-phenylpiperazine in 50 ml EtOH and heated at 50° for 5 hr to give 95.3% β-(1-phenyl-4-piperazinyl)propionic acid (2-nitro-4,5-dimethoxy)anilide, m. 167.5-8.5°. Over 100 similar compds. are described.
IT 26961-45-5P 27128-75-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 26961-45-5 CAPLUS
CN 1-Piperazinepropionanilide, 4',5'-dimethoxy-3-methyl-2'-nitro-4-phenyl- (8CI) (CA INDEX NAME)



RN 27128-75-2 CAPLUS
CN 1-Piperazinepropionanilide, 2'-bromo-4',5'-dimethoxy-3-methyl-4-phenyl- (8CI) (CA INDEX NAME)

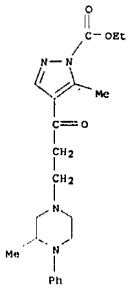


L9 ANSWER 108 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:78009 CAPLUS
DOCUMENT NUMBER: 70:78009
TITLE: N-[2-(Pyrazol-4-ylcarbonyl)ethyl]-N-arylpiperazines
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: Fr., 23 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1510206		19680119	FR 1966-87512	19661215 <--
US 3470184		19690930	US	19661222 <--
PRIORITY APPLN. INFO.:			CH	19651223
			CH	19661110

GI For diagram(s), see printed CA Issue.
AB Pyrazol-4-ylcarbonylethyl piperazines (I), useful as hypotensive agents, are prepared A mixture of 9.8 g. 4-acetyl-1-carbethoxy-5-methylpyrazole (II), 4.5 g. paraformaldehyde, 12.5 g. N-(2-methylphenyl)-piperazine-2HCl, 8 drops concentrated HCl, and 150 ml. EtOH is refluxed overnight to give N-[3-(1-carbethoxy-5-methyl-4-pyrazolyl)-3-oxo-propyl]-N'-(2-methylphenyl)piperazine, HCl salt m. 214-15° (decomposition). Similarly prepared are the following I (X = OEt, R = Me) (Ar and m.p. HCl salt given): o-ClC6H4, 215-16° (decomposition); p-FC6H4, 215° (decomposition); o-MeOC6H4, 202-3° (decomposition); o-EtC6H4, 190° (decomposition); p-tolyl, -, 2HCl salt m. 195° (decomposition); m-ClC6H4, 205° (decomposition); 2-pyridyl, -, maleate m. 170°; m-F3CC6H4, 190-1° (decomposition); p-ClC6H4,196-7° (decomposition); 4-pyridyl, -, maleate m. 176-7°; o-FC6H4, 290° (decomposition); o-F3CC6H4, 198° (decomposition); and the following compds. (salt m.p. given): I (X = OEt, R = Ph, Ar = p-FC6H4), maleate dihydrate 15 3-4°; I (X = Ph, R = Me, Ar = o-tolyl), HCl 188° (decomposition); 1-[2-(1-carbethoxy-5-methylpyrazol-4 - ylcarbonyl)ethyl] - 4 - phenyl - 3 - methylpiperazine, -; 1-[2-(1-carbethoxy-5-methylpyrazol - 4 - ylcarbonyl)-ethyl)-4-(p-fluorophenyl)-3-methyl - 1,4 - diazacycloheptane, -. Also prepared, according to known methods, are the following N-(R-substituted)-4-(o-chlorophenyl)piperazines (R and salt m.p. given): 3 - hydroxy - 3 - (1 - carbethoxy - 5 - methylpyrazol-4-yl)propyl, 2HCl 175° (decomposition); 3-ethoxy-3-(1-carbethoxy-5-methylpyrazol-4-yl)propyl, maleate monohydrate 155-6°; 3-(1-carbethoxy-5-methylpyrazol-4-yl)allyl, -; 3-(1-carbethoxy-5-methylpyrazol-4-yl)propyl, maleate 120-2°; 3-acetoxy-3-(1-carbethoxy-5-methylpyrazol-4-yl)propyl, HCl, -; and (m.p. given): II, 67° (thiosemicarbazone m. 212°, guanylhydrazone-HCl m. 206°); 4-benzoyl-1-carbethoxy-5-methylpyrazole, 79-82°.
IT 21635-26-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 21635-26-7 CAPLUS
CN Pyrazole-1-carboxylic acid, 5-methyl-4-[3-(3-methyl-4-phenyl-1-piperazinyl)propionyl]-, ethyl ester (8Cl) (CA INDEX NAME)

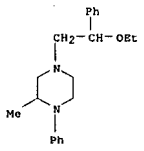


L9 ANSWER 109 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:443935 CAPLUS
DOCUMENT NUMBER: 69:43935
TITLE: 1-(2-Ethoxy-2-phenylethyl)-4-arylpiperazines
INVENTOR(S): De Stevens, George; Mull, Robert P.
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: Patentschrift (Switz.), 3 pp.
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

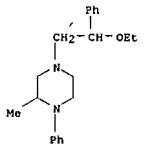
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 446350		19680315	CH 1964-5558	19640120 <--

GI For diagram(s), see printed CA Issue.
AB 2-MeOC6H4NH(CH2)2NH2 (69 g.) and 9.2 g. EtOCHPhCH2Cl in 250 ml. was refluxed 24 hrs. to give 2-MeOC6H4NH(CH2)2NHCH2CH(OEt)Ph, which (5 g.) in 40 ml. BuOH was refluxed 17 hrs. with 3 g. (CH2Br)2 and excess Na2CO3 to give 1-(2-ethoxy-2-phenylethyl)-4-(2-methoxyphenyl)piperazine (I) (R = 2-MeOC6H4, R1 = H); di-HCl salt m. 215-17° (EtOH-MeCN). Similarly prepared were the following I (R, R1, b.p./mm., salt, and m.p. salt given): Ph, H, 177-80°/0.35, di-HCl, 225-8°; 2-ClC6H4, H, 200-5°/0.55, HCl, 200-3° (EtOAc); Ph, Me, 165-80°/0.5, di-HCl, 230-5° (EtOH); 3-MeC6H4, H, 185-90°/0.2, di-HCl, 197-9° (EtOH); and 2-pyridyl, H, 185-90°/0.5, di-HCl, 125-30° (EtOH-Et2O). I show

antiinflammatory, antihypertensive, adrenolytic, diuretic, and saliuretic activity and are norepinephrine antagonists.
IT 853-91-8P 853-92-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 853-91-8 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



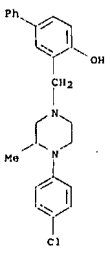
RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



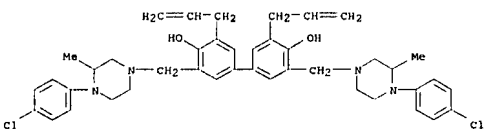
●2 HCl

L9 ANSWER 110 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:2801 CAPLUS
DOCUMENT NUMBER: 68:2801
TITLE: Potential anti-infective agents. I. Quinoline, phenolic, and β-aminoketone derivatives
AUTHOR(S): Magarian, Robert A.; Nobles, W. Lewis
CORPORATE SOURCE: Univ. of Mississippi, University, MS, USA
SOURCE: Journal of Pharmaceutical Sciences (1967), 56(8), 987-92
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.

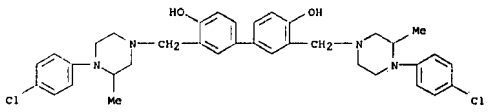
AB Mannich bases (e.g. I and II) were prepared, from quinolinols, isoquinolinols, phenols, biphenols, and ketones. Their antibacterial properties were evaluated. 25 references.
IT 16387-94-3P 16403-72-8P 16403-77-3P
16403-78-4P 16470-78-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 16387-94-3 CAPLUS
CN 4-Biphenylol, 3-[[4-(p-chlorophenyl)-3-methyl-1-piperazinyl]methyl]- (8CI) (CA INDEX NAME)



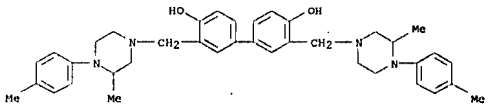
RN 16403-72-8 CAPLUS
CN [m,m'-Bitolyl]-4,4'-diol, 5,5'-diallyl-α,α'-bis[4-(p-chlorophenyl)-3-methyl-1-piperazinyl]- (8CI) (CA INDEX NAME)



RN 16403-77-3 CAPLUS
CN [m,m'-Bitolyl]-4,4'-diol, α,α'-bis[4-(p-chlorophenyl)-3-methyl-1-piperazinyl]- (8CI) (CA INDEX NAME)

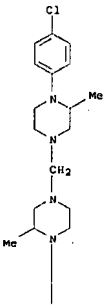


RN 16403-78-4 CAPLUS
CN [m,m'-Bitolyl]-4,4'-diol, α,α'-bis(3-methyl-4-p-tolyl-1-piperazinyl)- (8CI) (CA INDEX NAME)



RN 16470-78-3 CAPLUS
CN Piperazine, 1,1'-methylenebis[4-(p-chlorophenyl)-3-methyl- (8CI) (CA INDEX NAME)

PAGE 1-A



L9 ANSWER 111 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:104296 CAPLUS
DOCUMENT NUMBER: 64:104296
ORIGINAL REFERENCE NO.: 64:19641a-h,19642a
TITLE: Diazacycloalkanes
INVENTOR(S): Yost, William L.; Margerison, Richard B.
PATENT ASSIGNEE(S): CIBA Corp.
SOURCE: 10 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

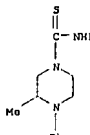
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3247206		19660419	US 1962-228760	19621005 <--
PRIORITY APPLN. INFO.:			US	19621005

GI For diagram(s), see printed CA Issue.
AB I-V, which can easily be prepared from R2R3CO, R1NH2, NaCN, and ClCHR4COCl, are treated with LiAlH4 to give VI-X. Similarly prepared are the corresponding diazacycloheptanes and diazacyclooctanes. To a solution of 830 g. NaHSO3 in 1540 ml. H2O was added during 1 hr. at 60-70° 352 g. AcH and, after 0.5 hr. stirring, 745 g. PhNH2 during 0.5 hr. Diluting with 200 ml. H2O, stirring 20 min., addg. 405 g. NaCN in 900 ml. H2O during 15 min. (temperature below 70°), and stirring 20 min. gave 61.5% N-(1-cyanoethyl)aniline (XI). To a mixture of 17.4 g. XI and 12.6 g. Na2CO3 in 87 ml. C6H6 was added 18.2 g. ClCH2COCl in 87 ml. C6H6 and the mixture refluxed 75 min. and kept overnight to give 95.7% I, m. 66-8°. A mixture of 11.37 g. LiAlH4 and 280 ml. tetrahydrofuran (THF) was refluxed under N 20 min. and cooled to 25°. After dropwise addition at 25° of 22.26 g. I in 85 ml. THF (18 min.), THF was distilled and replaced by PhMe, until during 50 min. 500 ml. distillate were collected. The mixture was refluxed 6 hrs., cooled to 25°, and quenched with 18 ml. H2O and 12.3 ml. 15% NaOH. After standing overnight, filtration, and evaporation, the residue was refluxed 2.5 hrs. with 8.5 g. Na2CO3 in 50 ml. PhMe to give 58.5% VI, b1 115-25°. Reaction of VI with an equimolar amount of PhNCS gave the phenylthiocarbamoyl derivative of VI, m. 158-60° (EtOH). A similar reduction of 222.6 g. I with 113.7 g. LiAlH4 led to 50% VI, b1 115-19°. Alternately, a mixture of 9.48 g. LiAlH4 and 22.26 g. I in 365 ml. THF was distilled and the THF replaced by xylene, until 340 ml. distillate was collected. The mixture was refluxed 6.75 hrs., cooled, treated with 15 ml. H2O and 10.25 ml. 15% NaOH, filtered, and evaporated. Refluxing the residue 2.5 hrs. with 8.5 g. Na2CO3 in 35 ml. PhMe gave 63.4% VI, b1 114-20°. To a suspension of 52.2 g. XI and 37.8 g. Na2CO3 in 482 ml. C6H6 was added dropwise during 10 min. 49.5 g. MeCHClCOCl in 100 ml. C6H6. The mixture was refluxed 2.5 hrs. and kept at room temperature overnight to give 70.4% II, m. 83-6°. Reduction of 23.65 g.

II with 11.37 g. LiAlH4 yielded 57.4% VII, b1, 117-25°; phenylthiocarbamoyl derivative m. 163-5° (EtOH). A mixture of 312.2 g. NaHSO3, 590 ml. H2O, and 43.5 g. Me2CO, prepared at 60-70°, was refluxed 45 min. and treated at 95° with 46.5 g. PhNH2. After 1 hr. reflux and addition of 100 ml. Me2CO and 29.5 g. NaCN in 65 ml. H2O, refluxing was continued 30 min. to give 68.8 g. N-(2-cyano-2-propyl)aniline (XII), m. 92-4° (50% EtOH). Refluxing 19.2 g. XII and 14.8 g. ClCH2COCl in C6H6 with Na2CO3 yielded III, m. 88-90° (AcOEt), which was dissolved in 85 ml. THF and added dropwise to 12 g. LiAlH4 in 300 ml. THF. The mixture was refluxed 6 hrs., quenched with 19 ml. H2O and 13 ml. 15% NaOH, filtered, and evaporated. The residue was refluxed 2.5 hrs. with Na2CO3 in PhMe to give 3.7 g. VIII, b1 110-15°; phenylthiocarbamyl derivative m. 193-5°. Refluxing a mixture of 29.2 g. XI and 27.7 g. Cl(CH2)2COCl 45 min. in C6H6 with 21.2 g. Na2CO3 gave crude N-(β-chloropropionyl)-N-(1-cyanomethyl)aniline (XIII), which was treated with 10.9 g. LiAlH4 in 385 ml. THF (6 hrs. reflux). Addition of 17.3 ml. H2O and 11.6 ml. 15% NaOH, filtration, evaporation, treatment of the residue with Na2CO3 in refluxing PhMe, and distillation gave 4.6 g. 2-methyl-1-phenyl-1,4-diazacycloheptane (XIV), b1 130-2°. Similarly, a solution of 34.2 g. XIII in 150 ml. THF was added to 16.15 g. LiAlH4 in 400 ml. THF at 37-40° and the mixture kept 2.5 hrs. to give 33.9% (based on XI) XIV, b1 118-20°. In this case, XIII was prepared from 29.2 g. XI, 27.7 g. Cl(CH2)2COCl, and 21.2 g. Na2CO3 in 350 ml. (ClCH2)2 by stirring 2.5 hrs. at -15° and keeping 16.5 hrs. at -35 to -40° to give a yield of 56.6 g. A mixture of 29.2 g. XI, 30 g. Cl(CH2)3COCl, and 21.2 g. Na2CO3 was refluxed 45 min. in C6H6 to give crude N-(γ-chlorobutyryl)-N-(1-cyanoethyl)aniline, which was treated with 10.9 g. LiAlH4 in 185 ml. THF (6 hrs. reflux) to give 10.4 g. 2-methyl-1-phenyl-1,4-diazacyclooctane, b1 138-42°. The reaction of paraformaldehyde with PhNH2 and HCN and treatment of the N-cyanomethylaniline with ClCH2COCl led to IV, which was treated with 3 equivs. LiAlH4 to give IX, b6 156°. Similarly, paraformaldehyde, iso-PrNH2, and KCN gave N-cyanomethyl-N-isopropylamine, which was treated with ClCH2COCl to give V. Reduction of V with 3 equivs. LiAlH4 furnished X, b. 156-63°. Reaction of H2C:CHCN with MeNH2 in the presence of a little PhCH2NMe3OH gave N-(2-cyanoethyl)-N-methylamine (XV), which was treated with ClCH2COCl. Reduction of the condensation product with LiAlH4 led to 1-methyl-1,4-diazacycloheptane, b32 71-3°. By reaction of XV with Cl(CH2)COCl and reduction of the condensation product with 3 equivs. LiAlH4 1-methyl-1,5-diazacyclooctane, b12 72-5°, was obtained. The new diazacycloalkanes are useful as anthelmintics and as intermediates for pharmaceuticals and germicides.
IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl- 4318-46-1P, 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio-
RL: PREP (Preparation)
(preparation of)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 4318-46-1 CAPLUS

CN 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio- (7CI, 8CI) (CA INDEX NAME)

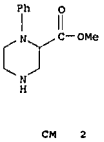


L9 ANSWER 112 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:59736 CAPLUS
DOCUMENT NUMBER: 64:59736
ORIGINAL REFERENCE NO.: 64:11149g-h,11150a-e
TITLE: 1,3-Cycloadditions of azomethinylides from aziridinecarboxylic esters
AUTHOR(S): Huisgen, Rolf; Scheer, Wolfgang; Szeimies, Guenter; Huber, Helmut
CORPORATE SOURCE: Univ. Munich, Germany
SOURCE: Tetrahedron Letters (1966), (4), 397-404
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB cf. Heine and Peavy, CA 63, 14796e. By a ring opening between the 2 and 3 positions, di-Me 1-(p-methoxyphenyl)aziridine-2,3-dicarboxylate (I) adds to C:C and C.tplbond.C compds. to give pyrrolidine or pyrroline derivs. Heating di-Me 1-(p-methoxyphenyl)-Δ2-1,2,3-triazoline-4,5-trans-dicarboxylate at 100° gives I as a 15:85 cis-trans mixture. The reactions and epimerizations of I presumably proceed through the intermediate formation of epimers of MeO2CCH: N+(p-MeOC6H4)C-HCO2Me. Heating di-Me fumarate (II) and I at 140° yields 94% tetra-Me 1(p-methoxyphenyl)pyrrolidine-2,3,4,5-tetracarboxylate (III)containing an oily isomer (IIIa) and 59% of a crystalline isomer (IIIb), m. 112-13°. IIIa and IIIb are dehydrogenated by chloranil (IV) in boiling Decalin to give 21 and 22% yields, resp., of tetra-Me 1-(p-methoxyphenyl)pyrrole-2,3,4,5-tetracarboxylate, independently synthesized by the method of Huntress, et al. (CA 50, 12977b) from p-MeOC6H4NHOH and (MeO2CC.tplbond.)2. III is also prepared in 61% yield from II and p-MeOC6H4N3 at 100-140°. At 120°, I and ((EtO2C)2CH:)2 give 77% of 2,5-di-Me 3,3,4,4-tetra-Et 1-(p-methoxyphenyl)pyrrolidine-2,3,3,4,4,5-hexacarboxylate containing 65% of the cis form, m. 114-15°, and 35% of the trans form, m. 114-16°, separated on silica gel by 9:1 C6H6-Et2O. The addition of norbornene to I at 100° gives 94% V containing 63% cis form (V, R = CO2Me, R1 = H), an oil, and 37% trans form (V, R = H, R1 = CO2Me), m. 87-9°, separated by thin layer chromatography. IV in boiling cymene converts V to VI, m. 161-2°. At 125°, I combines with HC.tplbond.CH in Me2CO to give an 81% yield of adducts, presumably a mixture of Δ2- and Δ3-pyrrolines which are dehydrogenated by IV in boiling xylene to give a 68% yield of di-Me 1-(p-methoxyphenyl)pyrrole-2,5-dicarboxylate, identical to the product obtained from p-MeOC6H4NH2 and

di-Me α,α'-dihydroxymuconate (Kuhn and Dury, CA 45, 7017a). BzC.tplbond.CPh and I at 100° yield 93% of an adduct dehydrogenated by IV in PhMe to give 55% di-Me ester of 3-benzoyl-1-(p-methoxyphenyl)-4-phenylpyrrole-2,5-dicarboxylic acid (VII). VII decarboxylates at 200° to give 3-benzoyl-1-(4-methoxyphenyl)-4-phenylpyrrole (VIII), characterized by its 2,4-dinitrophenylhydrazone. VIII is also prepared by condensing the Na derivative of BzCH2CHO with p-MeOC6H4NHCH2Br, and cyclizing the product with concentrated H2SO4. Photochem. or thermally (150°), I dimerizes to give a mixture from which two isomers, m. 188-9° and 240-1°, of tetra-Me 1,4-bis(p-methoxyphenyl)piperazine-2,3,5,6-tetracarboxylate have been isolated. Heating Me 1-phenylaziridine-2-carboxylate (IX) 6 hrs. at 200° gave 50% of the di-Me ester of 1,4-diphenylpiperazine-2,3-trans-dicarboxylic acid (X), m. 132-3°, and 5% of the cis ester, m. 105-6°. Distillation of Ca salt of X yields (PhNHCH2)2 and 1,4-diphenylpiperazine. The reaction of IX with trans-(BzCH:)2 (XI) gives a 1:1 adduct, m. 120-1°, and with PhCH:NMe, an adduct, m. 132.5-4° (structures not given). The addition of 1-benzyl-2,3-trans-dibenzoylaziridine to XI gives 34% of 1-benzyl-2,3,4,5-(all-trans)-tetrabenzoylpyrrolidine.
IT 5969-86-8P, Methylamine, N-benzylidene-, compound with Me 1-phenyl-2-aziridinecarboxylate (1:1)
RL: PREP (Preparation)
(preparation of)
RN 5969-86-8 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-, methyl ester, compd. with N-benzylidenemethylamine (1:1) (8CI) (CA INDEX NAME)

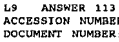
CM 1

CRN 46490-35-1
CMF C12 H16 N2 O2



CM 2

CRN 622-29-7
CMF C8 H9 N

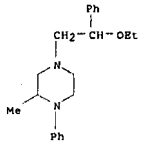


L9 ANSWER 113 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:416903 CAPLUS
DOCUMENT NUMBER: 63:16903
ORIGINAL REFERENCE NO.: 63:2985g-h
TITLE: 1-(2-Phenyl-2-ethoxyethyl)-4-phenylpiperazines
INVENTOR(S): De Stevens, George; Mull, Robert P.

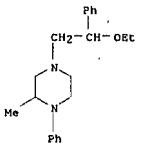
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 32 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 642845		19640722	BE	<--
FR 1404442			FR	
FR M3308			FR	
FR M3309			FR	
GB 1047044			GB	
PRIORITY APPLN. INFO.:			US	19630123

OTHER SOURCE(S): MARPAT 63:16903
GI For diagram(s), see printed CA Issue.
AB Compds. of the general formula I are prepared and can be used as antiinflammatory and diuretic agents. Thus, a mixture of 11.8 g. Ph(EtO)CHCH2Cl, 12.5 g. 1-(2-methoxyphenyl)piperazine, and 200 ml. BuOH is refluxed 24 hrs. in the presence of 40.0 g. Na2CO3 to give 1-(2-ethoxy-2-phenylethyl)-4-(2-methoxyphenyl)piperazine, b0.9 179-80°, 2HCl salt m. 215-17° (EtOH and MeCN). Also prepared are the following I (R, X, Y, b.p./mm., and m.p. 2HCl salt given): H, H, H, 177-80°/0.35, 225-8°; H, Cl, H, 200-5°/0.55, 200-3° (EtOAc); Me, H, H, 165-80°/0.5, 230-5° (EtOH); H, H, Me, 185-90°/0.2, 197-9° (EtOH). Also prepared are 1-(2-ethoxy-2-phenylethyl)-4-(2-pyridyl)piperazine (b0.5 185-90°, 2HCl salt m. 125-30° (EtOH and Et2O)), 1-(2-hydroxy-2-phenylethyl)-4-(2-methoxyphenyl)piperazine, (Cl CH2CH2)2NCH2CH(OEt)Ph.
IT 853-91-8P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- 853-92-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)
RN 853-91-8 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)

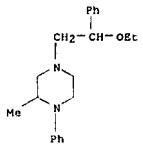


RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



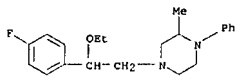
●2 HCl

L9 ANSWER 114 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:85303 CAPLUS
DOCUMENT NUMBER: 62:85303
ORIGINAL REFERENCE NO.: 62:15243g-h
TITLE: Anesthetic effect of some variants of mepivacaine (carbocaine). Preliminary studies and clinical impressions
AUTHOR(S): Feldmann, Gunter; Nordenram, Ake
CORPORATE SOURCE: Central Hosp., Karlstad, Swed.
SOURCE: J. Oral Therap. Pharmacol. (1965), 1(4), 421-7
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Carbocaine I (R = Me, R' = H) was clinically tested with analogs (Ekenstam, CA 52, 14609e) for local anesthetic activity. I (R = Et, R' = H) and I (R = H, R' = Me) were longer lasting than carbocaine, though the time of onset was somewhat longer.
IT 853-92-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride 1168-17-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride 2281-97-2P, Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)
RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



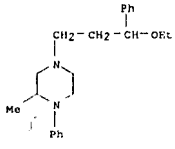
●2 HCl

RN 905-90-8 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



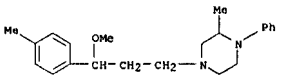
●2 HCl

RN 1168-17-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



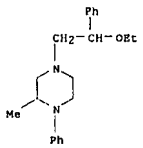
●2 HCl

RN 2281-97-2 CAPLUS
CN Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



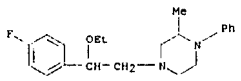
●2 HCl

L9 ANSWER 115 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:85302 CAPLUS
DOCUMENT NUMBER: 62:85302
ORIGINAL REFERENCE NO.: 62:15243f-g
TITLE: N,N'-Disubstituted compounds with diverse biological activities
AUTHOR(S): Mull, Robert P.; Tannenbaum, Carl; Dapero, Mary R.; Bernier, Marcel; Yost, William; De Stevens, George
CORPORATE SOURCE: CIBA Corp., Summit, NJ
SOURCE: Journal of Medicinal Chemistry (1965), 8(3), 332-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A large number of N,N'-disubstituted compds. were prepared for broad biol. testing. Some N-phenylpiperazine derivs. had antihypertensive, adrenolytic, and antiinflammatory properties. A structure-activity relation study was carried out to sep. these activities in single compds.
IT 853-92-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride 1168-17-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride 2281-97-2P, Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride 2946-76-1P, Piperazine, 2-methyl-1-phenyl-
RL: PREP (Preparation)
(preparation of)
RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



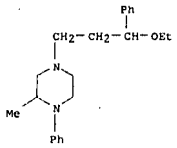
●2 HCl

RN 905-90-8 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



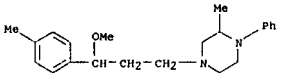
●2 HCl

RN 1168-17-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

RN 2281-97-2 CAPLUS
CN Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 116 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:85301 CAPLUS
DOCUMENT NUMBER: 62:85301
ORIGINAL REFERENCE NO.: 62:15243e-f
TITLE: Structure-activity relations in the field of antibacterial steroid acids
AUTHOR(S): Fried, Josef; Krakower, Gerald W.; Rosenthal, David; Basch, Harold
CORPORATE SOURCE: Squibb Inst. for Med. Res., New Brunswick, NJ
SOURCE: Journal of Medicinal Chemistry (1965), 8(3), 279-82
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antibacterial activity of a variety of steroidal and triterpenoid acids was determined using Staphylococcus aureus 209P as the test organism. Activity was less dependent on specific structural and stereo-chemical features than had been anticipated. All active compds. have a rigid polycyclic skeleton with a carboxyl group close to an O function or a double bond.
IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl-
RL: PREP (Preparation)
(preparation of)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

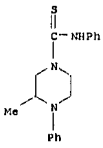
L9 ANSWER 117 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:74269 CAPLUS
DOCUMENT NUMBER: 62:74269
ORIGINAL REFERENCE NO.: 62:13159h,13160a-d
TITLE: Cyclic diaza compounds
INVENTOR(S): Yost, William L.; Margerison, Richard B.
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 48 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1378964		19641120	FR 1963-949434	19631003 <--
GB 1041086			GB	
PRIORITY APPLN. INFO.:			US	19621005

AB Compds. of the general formula X(CH2)nNR(CH2)mCN, in which X is halogen, m and n may be 1 or 2, and some or all C atoms may have alkyl or other groups, are cyclized by reduction with LiAlH4 or similar agents, hydrolysis, and heating with alkali. A solution of 11.37 g. LiAlH4 in 280 ml. tetrahydrofuran was added dropwise at 25° to 22.26 g. PhN(COCH2Cl)CHMeCN (I) in 85 ml. tetrahydrofuran. After the initial reaction subsided the solvent was distilled, and replaced by toluene. Distillation was continued at such a rate that 500 ml. total distillate was collected in 50 min. and pot temperature was 110° After 6 hrs. addnl. heating the mixture was cooled and poured into 15% NaOH solution After several hrs. the organic layer was washed and evaporated to dryness. The product was then refluxed in 50 ml. toluene with 8.5 g. Na2CO3 2 hrs., the solvent evaporated, and the 2-methyl-1-phenylpiperazine was distilled, b1 115-25°; 4-phenylthiocarbamatem. 158-60°(alc.). Aniline(745 g.) was slowly added at 60-70° to a solution of addition product of 352 g. AcH and 830 g. NaHSO3 in 1540 ml. water. The mixture was diluted with 200 ml. water and a solution of 405 g. NaCN in 900 ml. water was added in 15 min. The mixture was stirred 20 min., cooled to 10° and filtered and H2O added to give N-(1-cyanoethyl)aniline (II), m. 90-2° (alc.). A solution of 18.2 g. ClCH2COCl in 87 ml. benzene was slowly added to a mixture of 17.4 g. II in 87 ml. benzene and 12.6 g. Na2CO3. The mixture was boiled 75 min. and cooled, and after several hrs., filtered and evaporated The residue was dissolved in 200 ml. 50% aqueous alc. and cooled to -8° to give I, m. 66-8°. Similarly prepared were: 2,5-dimethyl-1-phenylpiperazine, b1 117-25° [phenylthiocarbamate m. 163-5° (alc.)], and the following piperazines (substituents given): 2,2-dimethyl-1-phenyl, b1, 110-15° [phenylthiocarbamate m. 193-5° (alc.)]; 1-isopropyl, b. 156-63°. Anilines prepared were (substituents given): N-(α-chloropropionyl)-N-(1-cyanoethyl), m. 83-6° (anhydrous EtOH); N-(2-cyano-2-propyl), m. 88-90° (EtOAc); N-(β-chloropropionyl)-N-(cyanoethyl). Other compds. prepared were: 2-methyl-1-phenyl-1,4-diazacycloheptane, b1 130-2°; 2-methyl-1-phenyl-1,4-diazacyclooctane, b1 138-42°; 1-methyl-1,4-diazacycloheptane, b32 71-3° ; 1-methyl-1,5-diazacyclooctane, b12 72-5°, [di-HBr salt m. 215-17° (alc.)]. Some of these compds. are useful as anthelmintic, germicidal, or adrenolytic agents. They are also accelerators for rubber mfg.
IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl- 4318-46-1P, 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio-

RL: PREP (Preparation)
(preparation of)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 4318-46-1 CAPLUS
CN 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio- (7CI, 8CI) (CA INDEX NAME)



L9 ANSWER 118 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:66601 CAPLUS
DOCUMENT NUMBER: 62:66601
ORIGINAL REFERENCE NO.: 62:11833a-d
TITLE: Substituted piperazines
INVENTOR(S): de Steven, George; Mull, Robert P.
PATENT ASSIGNEE(S): Ciba Soc.
SOURCE: 34 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1382425		19641218	FR 1964-959909	19640110 <--
BE 642429			BE	
PRIORITY APPLN. INFO.:			US	19630114

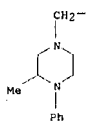
AB 3-Methyl 4-phenyl-1-(2-phenylthioethyl)piperazine di-HCl salt, m. 214-15° (EtOH-Et2O), was prepared by refluxing 7.04 g. 2-methyl-1-phenylpiperazine and 4.34 g. PhS(CH2)2Br in 75 cc. PhMe 6 hrs. Similarly were prepared 4-(2-methoxyphenyl)-1-(2-phenylthioethyl)piperazine di-HCl salt, m. 190-3° (PhMe-EtOH), 4-(2-methoxyphenyl)-1-[2-(4-tert-butylphenylthio)ethyl]-piperazine di-HCl salt, m. 200-5° (PhMe-EtOH), and 1-[2-(2-isopropylphenylthio)ethyl]-4-(2-methoxyphenyl)piperazine di-HCl salt, m. 200-5° (PhMe-EtOH). 4-Phenyl-1-(2-phenylthio-ethyl)piperazine di-HCl salt (I), m.

198-9° (EtOH) (free base b0.6 190-200°) was prepared by refluxing 5 g. PhS(CH2)2Br and 4.35 g. 1-phenylpiperazine in 200 cc. BuOH containing 10 drops H2O and 6 g. Na2CO3 92 hrs. I was also prepared by refluxing 7.65 g. PhS(CH2)2NH2 (II), 10.9 g. PhN[(CH2)2Cl]2 in 50 cc. MeOH, and excess K2CO3 15 hrs., or similarly using N,N-bis(2-chloro-ethyl)-N-(2-phenylthioethyl)amine (III) and 10 g. PhNH2. 2-(4-tert-Butylphenylthio)ethyl bromide, m. 176-7°, was prepared by adding 35.6 g. Cl(CH2)2OH to 55 g. 4-tert-butylthiophenol in 132 cc. 10% NaOH, stirring the solution 1 hr. at room temperature, and refluxing the mixture 30 min. to give 2-(4-tert-butylphenylthio)-ethanol b12 175-6° which (21 g.) was added dropwise to 10.84 g. PBr3 and 3 g. pyridine at 0° and stirred overnight. II was prepared by refluxing 46 g. PhS(CH2)2Br, 44 g. K phthalimide, and a few crysts. iodine in 80 cc. HCONHMe2 2 hrs., refluxing the crude product 2 hrs. with 20 g. N2H4 in 200 cc. MeOH, cooling, acidifying the solution with HCl, and refluxing 30 min. III was prepared by heating for 16 hrs. in a sealed tube 15.3 g. PhS(CH2)2NH2 and 9 g. (CH2)2O and adding 23.5 g. of the obtained N,N-bis(2-hydroxyethyl)-N-(2-phenylthioethyl)amine with cooling to 25 g. PCl5 in 100 cc. dry CHCl3 and refluxing the mixture 2-(2-Isopropylphenylthio)ethyl bromide, b12 157-8°, was prepared from 2-isopropylthiophenol and HOCH2CH2Cl and the product, 2-(2-isopropylphenylthio)ethanol, b1 130-5°, treated with PBr3 and C5H5N. The title compds, are antihypertensive and antiinflammatory agents.

IT 1039-99-2P, Piperazine, 2-methyl-1-phenyl-4-[2-(phenylthio)ethyl]-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 1039-99-2 CAPLUS

CN Piperazine, 2-methyl-1-phenyl-4-[2-(phenylthio)ethyl]-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 119 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:66597 CAPLUS
DOCUMENT NUMBER: 62:66597
ORIGINAL REFERENCE NO.: 62:11831c-h,11832a-d
TITLE: N-Aryl-N'-aralkyldiazacycloalkanes
INVENTOR(S): De Stevens, George; Mull, Robert P.
PATENT ASSIGNEE(S): CIBA Corp.
SOURCE: 14 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3168522		19650202	US 1963-315405	19631010 <--

PRIORITY APPLN. INFO.: US 19631010

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) have adrenolytic, antihypertensive, antiinflammatory, diuretic, saliuretic, analgesic, and antifibrillatory properties. To a solution of 8.8 g. 2-methyl-1-phenylpiperazine in 50 ml. toluene was added 2.4 g. of a mineral oil suspension (53%) of NaH. The mixture was refluxed 2 hrs. and then refluxed overnight with 11.6 g. 3-ethoxy-3-(4-methylphenyl)propyl chloride. After filtering off inorg. material, the filtrate was distilled to yield 1-[3-ethoxy-3-(4-methylphenyl)propyl]-3-methyl-4-phenylpiperazine, b0.2 182-4°; dihydrochloride m. 190-2°. In this manner were prepared the I (n = 2) given in the first table. Crude 3-(4chlorophenyl)-3-ethoxypropylamine (II) was prepared from 50 g. 3-(4-chlorophenyl)-3-ethoxypropyl chloride and 44 g. K phthalimide in 80 ml. dimethylformamide. m.p., R, R1, R2, R3, b.p./mm., m.p. di-HCl salt, Et, H, Me, H, 168-70°/0.075, 194°; iso-Pr, 4-Me, Me, H, 146-54°/0.04, 169°; Me, 4-Me, H, H, 170-2°/0.05, 200°; Et, 4-Me, H, H, 196°/0.04, 194°; Et, 4-Me, H, 3-Me, 172-4°/0.04, 165°; Me, 4-Me, Me, H, 176-8°/0.1, 197-8°; Me, 4-Me, H, 2-Me, 180-2°/0.12, 163°; Me, 4-Me, H, 2-Cl, 182-4°/0.05, 153-5°; Me, 4-Me, H, 3-Me, 174-8°/0.07, 155°; iso-Pr, 4-Me, H, 2-Me, 176-80°/0.04, 171-3°; iso-Pr, 4-Me, H, 2-Cl, 194-200°/0.04, 159°; iso-Pr, 4-Me, H, 4-Me, 190-2°/0.09, 173°; Et, H, H, 2-Cl, 176-8°/0.03, 141-3°; Me, 4-Me, H, 4-Me, 208-12°/0.09, 192°; Et, H, H, 4-Cl, 238-40°/0.08, 155°; Et, H, H, 2-Me, 180-2°/0-2, 150-4°; Et, H, H, 4-Me, 180-3°/0.2, 200°; Et, H, H, 4-OMe, --, 210-11°; Et, H, H, H, 160°/0.15, 202-3°; Et, 4-Cl, H, H, 168°/0.1, 208°; Et, 4-Cl, Me, H, 206-8°/0.07, 192°; Et, 4-Me, H, H, 186°/0.05, 164-6°; Et, 4-Me, H, 2-Cl, 184-6°/0.04, 150-2°; Et, 4-Me, H, 2-Me, 222-4°/0.14, 186°; Et, 4-Me, H, 3-Cl, 208-10°/0.06, 168-70°; Me, 4-Me, H, 2-OMe, --, 175-7°; Et, 4-Cl, H, 4-Cl, 214-16°/0.11, 188°; Et, 4-Cl, H, 3-OMe, 204-6°/0.12, 165°; Me, 4-Cl, Me, H, 170-8°/0.05, 184°; Et, 4-Cl, H, 4-Me, 196-200°/0.04, 197°; iso-Pr, 4-Cl, H, H, 198-200°/0.09, 200°; Me, 4-Cl, H, H, 192-4°/0.08, 215°; Me, 4-Cl, H, 4-Me, 186-90°/0.09, 195°; Me, 4-Cl, H, 2-Me, 208-10°/0.17, 165°; Et, 4-Cl, H, 3-Me, 180-2°/0.04, 173°; Et, 4-Me, H, 4-Me, 192-6°/0.011, 194-5°; Et, 4-Me, H, 4-Cl, --, 174-6°; Et, 4-Cl, H, 2-Me, 198-202 °/0.16, 184°; Et, 4-Cl, H, 2-Cl, 210-12°/0.07, 120°; Et, 4-Cl, H, 3-Cl, 206-8°/0.06, 169°; Et, 2-Cl, H, H, 182-4°/0.08, 170°; Et, 4-Me, H, 2-Me, 186°/0.05, 164-6°; Et, H, H, 3-Me, 172-4°/0.05, 166°; Et, 4-Cl, H, 2-OMe, 206-10°/0.13, 200°; Et, H, H, 3-OMe, --, 163°; N,N-bis(2-chloroethyl)-N-(2-chlorophenyl)amine (III) was prepared by heating a mixture of 2-chloroaniline and ethylene oxide in a sealed tube and converting the resulting N-(2-chlorophenyl)-N,N-bis(2-hydroxyethyl)amine to III with SOCl2. A mixture of 21.3 g. II and 25.2 g. III in 100 ml. MeOH was refluxed with excess K2CO3 15 hrs. to give I. A mixture of 2490 g.

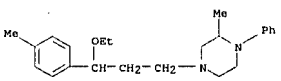
1-(2-methylphenyl)piperazine dihydrochloride, 285 g. paraformaldehyde, and 1735 g. 4-methylacetophenone in 7500 ml. EtOH was refluxed 24 hrs. with stirring and cooled to -10° and the precipitate filtered off and washed 3 times with 1000 ml. cold acetone to give 2850 g. 1-[3-(4-methylphenyl)-3-oxopropyl] -4-(2-methylphenyl)piperazine hy-drochloride (IV), m. 209-11°. Reduction of 2660 g. IV with 407 g. NaHB4 gave 2530 g. 1-[3-hydroxy-3-(4-methylphenyl)propyl]-4-(2-methylphenyl)piperazine (V), m. 80-3°. A solution of 2530 g. V in 19 ml. benzene was gassed with HCl to a pH of 2 and treated with 2750 g. SOCl2 in 12 ml. benzene, the mixture refluxed 2 hrs., and the remaining SOCl2 and benzene were distilled The residue in 12 ml. EtOH was held below 15° while adding 718 g. Na in 23 ml. EtOH and then refluxed 1 hr. The solution was evaporated to dryness and the residue dissolved in 80 ml. water and extracted with CHCl3 to yield 2700 g. 1-[3-ethoxy-3-(4-methylphenyl)propyl]-4-(2-methylphenyl)piperazine which gave a dihydrochloride m. 165-8°. The Grignard reagent from 76.4 g. 4-chlorobromo-benzene and 8.16 g. Mg condensed with 48.0 g. 1,2-dichlorodiethyl ether gave 2-(4-chlorophenyl)-2-ethoxyethyl chloride (VI), b12 122-40°. Condensation of VI with aryl piperazines by refluxing 24 hrs. in the presence of Na2CO3 gave I. In this manner were prepared I (n = 1), given in the second table. Also prepared R, R1, R2, R3, b.p./mm., m.p.di-HCl salt; Et, 4-Cl, H, 2-OMe, 190-200°/0.3, 229-31°; Et, 4-Cl, H, H , 90-1°/0. 3, 203-5°; Et, H, H, 2-OMe, 179-80°/0.9, 215-17°; Et, H, H, H, 177-80°/0. 35. 225-8°; Et, 3-CF3, H, H, 128-40°/0.35, 182-5°; Et, H, H, 2-Cl, 200-5°/0. 55, 200-3°; Et, H, Me, H, 165-80°/0.5, 230-5°; Et, 3,4-Cl2, H, 2-OMe, 210-20°/0.7, 221-5°; Et, 4-Cl, H, 2-Cl, 185-90°/0.2, 240-4°; Et, 3,4-Cl2, H, H, 210-20°/0.7, 211-13°; Et, 3-Cl, H, 2-OMe, 170-90°/0.7, 213-17°; Et, 3-Cl, H, H, 180-200°/0.7, 192-3°; Et, H, H, 3-Me, 185-90°/0.2, 197-9°; Et, 4-F, H, 3-Me, 160-85°/0.8, 193-60°; Et, 4-F, Me, H, 170-5°/0.6, 228-32°; Were the following VII (n, R, b.p./mm., and m.p. di-HCl salt given): 1, H, 185-90°/0.5, 125-30°; 2, 4-Me, 162-3°/0.25, 194-5°.

IT 442-26-2P, Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 745-59-5P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- 745-60-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl- 748-03-8P, Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 853-91-8P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- 853-92-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride 905-91-9P, Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, hydrochloride 905-92-0P, Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl- 907-68-6P, Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride 978-11-0P, Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl-, dihydrochloride 1049-29-2P, Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 1051-75-8P, Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl- 1051-76-9P, Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl-, dihydrochloride 1168-17-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride 3792-38-9P, Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)

(preparation of)

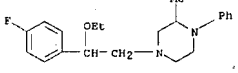
RN 442-26-2 CAPLUS

CN Piperazine, 4-[3-ethoxy-3-(4-methylphenyl)propyl]-2-methyl-1-phenyl- (9CI) (CA INDEX NAME)



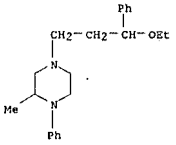
RN 745-59-5 CAPLUS

CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



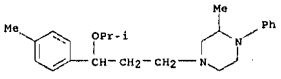
RN 745-60-8 CAPLUS

CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



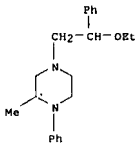
RN 748-03-8 CAPLUS

CN Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)

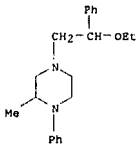


RN 853-91-8 CAPLUS

CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)

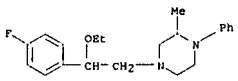


RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



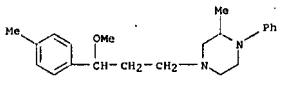
●2 HCl

RN 905-90-8 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



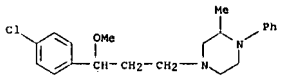
●2 HCl

RN 905-91-9 CAPLUS
CN Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, hydrochloride (7CI, 8CI) (CA INDEX NAME)

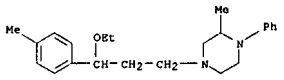


● HCl

RN 905-92-0 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl- (8CI) (CA INDEX NAME)

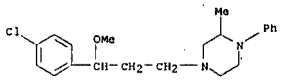


RN 907-68-6 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



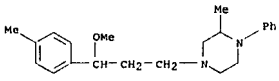
●2 HCl

RN 978-11-0 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

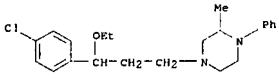


●2 HCl

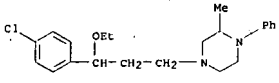
RN 1049-29-2 CAPLUS
CN Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 1051-75-8 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)

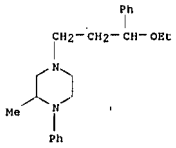


RN 1051-76-9 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



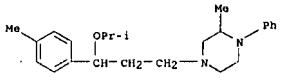
●2 HCl

RN 1168-17-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

RN 3792-38-9 CAPLUS
CN Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 120 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:43961 CAPLUS
DOCUMENT NUMBER: 62:43961
ORIGINAL REFERENCE NO.: 62:7777f-h
TITLE: Piperazinoalkyl esters of 9-hydroxyfluorene-9-carboxylic acid
INVENTOR(S): Biel, John H.
PATENT ASSIGNEE(S): Colgate-Palmolive Co.
SOURCE: 3 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

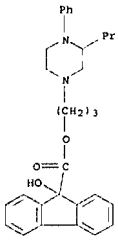
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3162637		19641222	US 1960-14502	19600314 <---
PRIORITY APPLN. INFO.:			US	19600314

GI For diagram(s), see printed CA Issue.
AB The title compds. (I), in which Y is alkylene and R is alkyl or aryl, were made. Thus, a mixture of 21.7 g. Me 9-hydroxy-fluorene-9-carboxylate, 14.2 g. N-methyl-N1-(3-hydroxypropyl)-piperazine, 0.5 g. MeONa, and 250 cc. heptane was refluxed 6 hrs., during which time 5.3 cc. MeOH was collected. The catalyst was then filtered off and the filtrate washed by H2O to yield

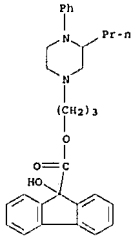
33.1 g. I [Y = (CH2)3, R = Me]; di-HCl salt m. 237° (decomposition) (MeOH). Similarly prepared were I (Y, R, and m.p. of di-HCl salt given): MeCHCH2, Me, 234° (decomposition); MeCHCH2, Ph, 239° (decomposition) (II). These I have ataractic effects and induce mild muscle relaxation. II is an antispasmodic.

IT 1864-47-7P, Fluorene-9-carboxylic acid, 9-hydroxy-, 3-(4-phenyl-3-propyl-1-piperazinyl)propyl ester 2083-58-1P, Fluorene-9-carboxylic acid, 9-hydroxy-, 3-(4-phenyl-3-propyl-1-piperazinyl)propyl ester, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 1864-47-7 CAPLUS
CN Fluorene-9-carboxylic acid, 9-hydroxy-, 3-(4-phenyl-3-propyl-1-piperazinyl)propyl ester (7CI, 8CI) (CA INDEX NAME)



RN 2083-58-1 CAPLUS
CN Fluorene-9-carboxylic acid, 9-hydroxy-, 3-(4-phenyl-3-propyl-1-piperazinyl)propyl ester, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 121 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:22615 CAPLUS
DOCUMENT NUMBER: 62:22615
ORIGINAL REFERENCE NO.: 62:4038g-h,4039a
TITLE: Piperazine-bithionol anthelmintic
INVENTOR(S): Gillingham, James M.; Clark, John C.
PATENT ASSIGNEE(S): Diamond Laboratories, Inc.
SOURCE: 2 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

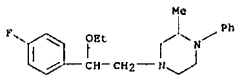
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3152041		19641006	US 1961-112533	19610525 <--
PRIORITY APPLN. INFO.:			US	19610525

GI For diagram(s), see printed CA Issue.
AB Piperazine-bithionol (piperazine-bithionolate) (I), m. 214-15°, having a wider spectrum of activity against parasitic infections in a large variety of animals than either of its precursors or salts is prepared from various ratios of piperazine (II) to bithionol (III) in acetone solution or precipitated from aqueous alkaline solution by acid. Thus, to 17.2 g. II anhydrous base in 250 ml. acetone was added 36.6 g. III in 250 ml. acetone in 5-ml. increments with mixing; crystals appeared at pH 10.5, and I crystallized at the end of the addition in 27-g. yield after separation and drying. It can be recrystd. from BuOH. In aqueous alkali, I had uv absorption values E1%1cm. maximum 236 at 327 mμ and min. 58 at 285 mμ. The L.D.50 (in mice) of I, II citrate, III, and II citrate-III is, resp.: 800, 4000, 3190, 1007 mg./kg. Two cats given 10 times the normal therapeutic dose of 150 mg./lb. I as an oral suspension showed no adverse effects, and 2 of 3 cats given 10 times the therapeutic dose in capsules showed only fecal softening and very slight tranquilization. I in doses of 150 mg./lb. for

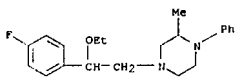
ascarid infection caused 100% egg reduction in dogs and 91% in cats; in one cat with hookworms the egg reduction was 70%.

IT 745-59-5P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 745-59-5 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 905-90-8 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 122 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:22614 CAPLUS
DOCUMENT NUMBER: 62:22614
ORIGINAL REFERENCE NO.: 62:4038e-g
TITLE: Medicinal piperazine compounds
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 18 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

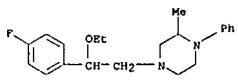
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6400467		19640724	NL 1964-467	19640122 <--
BE 642844			BE	
FR 1385772			FR	
PRIORITY APPLN. INFO.:			US	19630123

GI For diagram(s), see printed CA Issue.
AB The title compds. (I) show antipyretic, antiinflammatory, hypotensive, adrenolytic, and diuretic properties; they are norepinephrine antagonists.

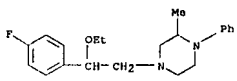
A mixture of 10.05 g. 1-(2-methoxyphenyl)piperazine, 11.5 g. 2-(4-chlorophenyl)-2-ethoxyethyl chloride (II), and 40.0 g. Na2CO3 in 200 ml. BuOH is refluxed 24 hrs. with stirring. After separation of the inorg. material, the filtrate is evaporated and the residue distilled to give I (X = 4-Cl, R2 = Et, R1 = H, Ar = 2-MeOC6H4), b0.3 190-200°; di-HCl salt m. 229-31° (iso-PrOH). II (b12 122-40°) is prepared by a Grignard reaction from 8.16 g. Mg in 75 ml. Et2O, 76.4 g. 4-ClC6H4Br, and 48 g. ClCH2CHClOEt. Similarly are prepared the following I (X, R2, R1, Ar, b.p./mm., and m.p. di-HCl salt listed): 4-Cl, Et, H, Ph, 90-1°/0.3, 203-5° (MeCN); 3-CF3, Et, H, Ph, 128-40°/0.35, 182-5°; 3,4-Cl2, Et, H, 2-MeOC6H4, 210-20°/0.7, 221-5° (Et2O, EtOH); 4-Cl, Et, H, 2-ClC6H4, 210-20°/0.7, 211-13° (Et2O, EtOH); 3-Cl, Et, H, 2-MeOC6H4, 170-90°/0.7, 213-17° (Et2O, EtOH); 3-Cl, Et, H, Ph, 180-200°/0.7, 191-3° (Et2O, EtOH); 4-F, Et, H, 3-MeC6H4, 160-5°/0.8, 193-6° (Et2O, EtOH); 4-F, Et, 3-Me, Ph, 170-5°/0.6, 228-32° (Et2O, EtOH).

IT 745-59-5P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 745-59-5 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 905-90-8 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



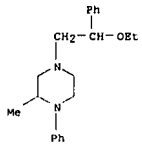
●2 HCl

L9 ANSWER 123 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:15362 CAPLUS
DOCUMENT NUMBER: 62:15362
ORIGINAL REFERENCE NO.: 62:2782f-h
TITLE: Piperazines
PATENT ASSIGNEE(S): CIBA Ltd.

SOURCE: 17 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

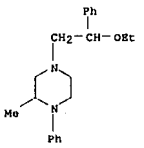
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6400466		19640724	NL 1964-466	19640122 <--
PRIORITY APPLN. INFO.:			US	19630123

GI For diagram(s), see printed CA Issue.
AB I were prepared by refluxing 11.8 g. EtOPhCHCH2Cl and 12.5 g. N-(2-methoxyphenyl)piperazine in 200 ml. BuOH containing 40 g. Na2CO3 24 hrs., the inorg. material filtered, and the filtrate evaporated to give I (R = 2-MeOC6H4, R1 = H), bo.9 179-80°; di-HCl salt m. 215-17° (EtOH-MeCN). The following I were similarly prepared (R, R1, b.p./mm., m.p. hydrochloride, and crystallization solvent given): Ph, H, 177-80°/0.35, 225-8° (di-HCl salt), --; 2-ClC6H4, H, 200-5°/0.55, 200-3°, AcCH2CO2Et; Ph, Me, 165-80°/0.5, 230-5°, EtOH; 3-MeC6H4, H, 185-90°/0.2, 197-9°, EtOH; 2-pyridyl, H, 185-90°/0.5, 125-30°, EtOH-Et2O. I, their N-oxides, and quaternary salts can be used as antiinflammatory or vasodilation agents.
IT 853-92-9
(Derived from data in the 7th Collective Formula Index (1962-1966))
RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

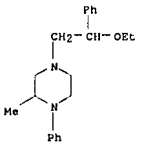


●2 HCl

IT 853-91-8P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- 3020-53-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, hydrochloride
RL: PREP (Preparation)
(preparation of)
RN 853-91-8 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 3020-53-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, monohydrochloride (8CI) (CA INDEX NAME)



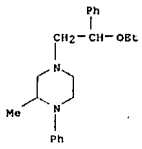
● HCl

L9 ANSWER 124 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:15361 CAPLUS
DOCUMENT NUMBER: 62:15361
ORIGINAL REFERENCE NO.: 62:2782e-f
TITLE: Diisopropylamine orotate
INVENTOR(S): Masusawa, Kuniyasu; Irikura, Tsutomu
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd.
SOURCE: 1 p.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 39008847	B4	19640528	JP	19610304 <--
PRIORITY APPLN. INFO.:			JP	19610304

AB A solution of 4 g. orotic acid in 20 cc. H2O is stirred with 2.59 g. diisopropylamine and evaporated in vacuo at below 50° to give 5.7 g. title compound, plates, m. 210-15°, useful as a H2O-soluble orotic acid derivative
IT 853-92-9
(Derived from data in the 7th Collective Formula Index (1962-1966))

RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



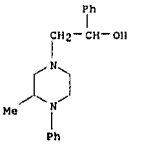
●2 HCl

L9 ANSWER 125 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:425459 CAPLUS
DOCUMENT NUMBER: 61:25459
ORIGINAL REFERENCE NO.: 61:4373f-h,4374a
TITLE: Quaternary salts of 5-(4-alkylpiperazino)dibenzo[a,d]cycloheptadienes
INVENTOR(S): Rhone-Poulenc, S. A.
SOURCE: 15 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 633454		19631210	BE	<--
DE 1197891			DE	
FR 1403619			FR	
FR CAM61			FR	
GB 1041536			GB	
NL 294074			NL	
US 3257404		19660621	US 1963-285859	19630606 <--
PRIORITY APPLN. INFO.:			FR	19620615

GI For diagram(s), see printed CA Issue.
AB 5-(4-Alkylpiperazino)dibenzo[a,d]cycloheptadienes (I) were converted to quaternary salts (II) with Me2SO4. These compds. showed spasmolytic, ganglioplegic, and atropinic activities more pronounced than the corresponding I. 5-Chlorodibenzo[a,d]cycloheptadiene (Mychajiyszyn and Protiva, CA 54, 8766a) (9.14 g.) in 150 cc. anhydrous PhMe was refluxed 4 h. with 8.00 g. 1-methylpiperazine in 30 cc. PhMe, the reaction mixture treated with 120 cc. water, 80 cc. Et2O, and 5 cc. aqueous NaOH (d. 1.33), the water layer washed with 100 cc. Et2O, the combined organic layers extracted 3 times with a total 440 cc. 2N NaOH, the acid exts. washed with 150 cc. Et2O and basified with 50 cc. aqueous NaOH (d. 1.33) and 50 cc. water, the resulting oil extracted 3 times with a total 400 cc. Et2O, and the combined Et2O exts. dried over K2CO3 and evaporated to yield 6.45 g. I (R = Me) (III), m.

111° (iso-PrOH). To 9.9 g. III in 200 cc. anhydrous Me2CO was added dropwise in 10 min. 4.3 g. Me2SO4 in 10 cc. anhydrous Me2CO, the temperature rising to 27°. The mixture was cooled to room temperature in 3 h. to yield 11.9 g. II (R = Me), m. 190-3°, washed twice with a total 70 cc. anhydrous Me2CO. Similarly prepared were the following homologs (R, m.p. of I, and m.p. of II given): Et, 90°, 168-70°; Pr, 84°, 201-3°; Bu, 78°, 207-9°; HOCH2CH2, 129°, 144-6°; PhCH2, 120-1°, 218-22°; iso-Pr, 87°, 201-3°; cinnamyl, 142°, 214-16°; PhCH2CH2, 99-100°, 160-70°; HOCH2CH2OCH2CH2, - (di-HCl salt m. 170°), 150°.
IT 94437-01-1P, 1-Piperazineethanol, 3-methyl-α,4-diphenyl-
RL: PREP (Preparation)
(preparation of)
RN 94437-01-1 CAPLUS
CN 1-Piperazineethanol, 3-methyl-α,4-diphenyl- (7CI) (CA INDEX NAME)



L9 ANSWER 126 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:425458 CAPLUS
DOCUMENT NUMBER: 61:25458
ORIGINAL REFERENCE NO.: 61:4373b-f'
TITLE: 2-(4-Phenylpiperazino)-1-phenylethyl acetates
INVENTOR(S): Shapiro, Seymour L.; Freedman, Louis; Soloway, Harold
PATENT ASSIGNEE(S): U.S. Vitamin & Pharmaceutical Corp.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

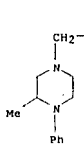
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3135756		19640602	US	19610517 <--
PRIORITY APPLN. INFO.:			US	19610517

GI For diagram(s), see printed CA Issue.
AB The title esters are prepared and can be used as bronchodilators. Thus, a solution of 17.8 g. 1-phenylpiperazine in 35 ml. iso-PrOH is added to a mixture of 25 g. p-ClC6H4COCH2Br in 65 ml. iso-PrOH and the mixture refluxed 15 min. to give 61% 1-(p-chlorophenacyl)-4-phenylpiperazine-HBr (I.HBr), m. 242-4° (decomposition) (MeOH), which is treated with NaOH to give I, m. 132-3° (EtOH). A mixture of 11.9 g. I in 100 ml. EtOH is treated with 0.65 g. NaBH4 to give 58% 2-(4-phenylpiperazino)-1-(p-chlorophenyl)ethanol (II), m. 154-5° (EtOH). A mixture of 3.2 g. II,

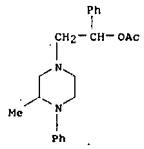
20 g. Ac2O, and 25 ml. MeCN is refluxed 9 hrs. to give 57% 2-(4-phenylpiperazino)-1-(p-chlorophenyl)ethyl acetate, m. 109-10° (hexane). Similarly prepared are the following III (X = CHOAc)(R, R1, and m.p. or b.p./mm. given): H, H (IV), 113-15°; (X = CHO2CEt) H, H, 132-4°/0.005; (X = CH2O2CPr) H, H, 186-90°/0.05; (X = CHOBz), H, H, [HCl salt m. 130-3° (Me2CO)]; (X = CHO2CNH2) H, H, 184-5°; (X = CHO2CNHEt) H, H, 126-7° (MeCN); H, p-Cl, 109-10°; H, p-Br, 118-19°; H, 2,4-Me2, 100-1°; o-Me, H, 99-101°; m-Me, H, 109-10°; p-Me, H, 88-9°; o-Cl, H, 90-1°; m-Cl, H, 95-7°; p-Cl, H, 123-4°; o-MeO, H, 200-6°/0.005; p-MeO, H, 87-8°. Also prepared is the analog of IV derived from 1-phenyl-2-methylpiperazine (IVa), m. 68°. Also prepared are the following III (X = CHOH) (R, R1, and m.p. or b.p./mm. given): H, H (V), 113° [HCl salt m. 184-5° (EtOH)]; o-Me, H, 116-17°; m-Me, H, 95-7°; p-Me, H, 118-19°; o-Cl, H, 129-30° m-Cl, H, 97°; p-Cl, H, 113-14°; o-MeO, H, 196-201°/0.01; p-MeO, H, 144°; H, p-Cl, 154-5°; H, p-Br, 160°; H, 2,4-Me2, 139-40°; H, p-Ph, 180° (MeCN). Also prepared is the analog of V derived from IVa, m. 109-10°. Also prepared are the following III (X = CO, R = H) (R1 and m.p. given): p-Br, 139-40° (EtOH) [HBr salt m. 243-6° (decomposition) (MeOH)]; 2,4-Me2, 110-11° (EtOH), p-Ph, 196-8° (MeCN).

IT 94437-01-1P, 1-Piperazineethanol, 3-methyl-α,4-diphenyl-
97018-29-6P, 1-Piperazineethanol, 3-methyl-α,4-diphenyl-, acetate (ester)
RL: PREP (Preparation)
(preparation of)

RN 94437-01-1 CAPLUS
CN 1-Piperazineethanol, 3-methyl-α,4-diphenyl- (7CI) (CA INDEX NAME)



RN 97018-29-6 CAPLUS
CN 1-Piperazineethanol, 3-methyl-α,4-diphenyl-, acetate (7CI) (CA INDEX NAME)



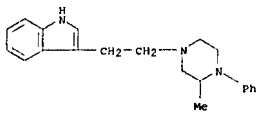
L9 ANSWER 127 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:52797 CAPLUS
DOCUMENT NUMBER: 60:52797
ORIGINAL REFERENCE NO.: 60:9296b-d
TITLE: Aminochloro heterocyclic compds.
INVENTOR(S): Weidinger, Hans; Wellenreuther, Gerhard; Bilingsfeld, Heinz
PATENT ASSIGNEE(S): Badische Anilin- & Soda-Fabrik A.-G.
SOURCE: 19 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
FR 1342841		19631115	FR 1962-909333	19620913	<--
DE 1172266			DE		
GB 1011984			GB		
PRIORITY APPLN. INFO.:			DE	19610913	

GI For diagram(s), see printed CA Issue.
AB The new compds. were used as intermediates in the manufacture of dyes. A mixture containing 100 parts by weight 2-(4-nitrophenyl)-4-chloroquinazoline suspended in 100 parts by volume Me2CO, 10 parts Raney Ni, and 3 parts by volume Pr3N was hydrogenated at normal pressure at 20-30° to yield 88 parts I (R = H, R1 = p-C6H4NH2). Similarly prepared were 85 parts I (R = H, R1 = m-C6H4NH2) from 100 parts 2-(3-nitrophenyl)-4-chloroquinazoline, and 85 parts I (R = NH2, R1 = Ph) from 100 parts 2-phenyl-4-chloro-6-nitroquinazoline. Also prepared were the following II (R and R1 given): morpholino, m-C6H4-NH2; morpholino, m-C6H4NO2, m. 200-2°; anilino, m-C6H4NH2; anilino, m-C6H4NO2, m. 164-5°; Ph, m-H2NC6H4NH; Ph, m-O2NC6H4NH, 197-9°; morpholino, p-H2NC6H4NH; morpholino, p-O2NC6H4NH, 255-7°.

IT 94961-31-6
(Derived from data in the 7th Collective Formula Index (1962-1966))

RN 94961-31-6 CAPLUS
CN Indole, 3-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (7CI) (CA INDEX NAME)



L9 ANSWER 128 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:52796 CAPLUS
DOCUMENT NUMBER: 60:52796
ORIGINAL REFERENCE NO.: 60:9293g-h,9294a-h,9295a-h,9296a-b
TITLE: Indolylpiperazines
PATENT ASSIGNEE(S): Sterling Drug Inc.
SOURCE: 41 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
GB 944443		19631211	GB		<--
US 3188313		19650608	US 1959-842203	19590925	<--
PRIORITY APPLN. INFO.:			US	19590925	

GI For diagram(s), see printed CA Issue.
AB Compds. of type I and II, in which R1 is H, halogen, alkyl, alkoxy, or aryl, R2 is H, alkyl, hydroxyalkyl, or aryl, R3 and R4 is H, alkyl, or aryl, n is 1 to 7, and in which the indole group may be joined in the 2-position or (as shown) the 3-position, were made. These are useful as hypotensive agents, as antinauseants, antipyretics, sedatives, tranquilizers and muscle relaxants; they inhibit apomorphine-induced vomiting, and prolong the narcosis of ether and barbiturates. A solution of 177 g. (PhCH2)2NCH2CH2NHPh, 120 g. ClCH2COCl and 650 m. CHCl3 was refluxed for 5.5 hrs. to yield 190 g. (PhCH2)2NCH2CH2NPhCOCH2Cl, an oil. This was dissolved in EtOCH2CH2OH, the solution refluxed 4 hrs., cooled, diluted with 650 ml. absolute EtOH, 4 g. Pd-C added, and the mixture reduced by H at 50 lb./in.2 to give 1-phenyl-2-piperazinone (VI), m. 100-5° (p-toluenesulfonate m. 220.2-4.6°). Similarly made from (PhCH2)2NCH2CH2N(4-ClC6H4)(COCH2Cl) (HCl salt m. 161.0-3.8°) was 1-(4-chlorophenyl)-2-piperazinone (HCl salt m. 192.8-4.8°); from 4-benzyl-1-(2,6-dimethylphenyl)-2-piperazinone (HCl salt m. 248.8-54.8°), 1-(2,6-dimethylphenyl)-2-piperazinone (HCl salt m. 224.8-6.0). The I and II were made by various methods. Method A: A mixture of 5.6 g. 2-(3-indolyl)ethyl bromide (VII), 4.1 g. 1-phenylpiperazine, 2.1 g. NaHCO3, and 30 ml. absolute EtOH was refluxed for 6 hrs. to yield 1.4 g. I (R1 = R3 = R4 = H, R2 = Ph, n = 2), m. 131.6-6.0°. Similarly prepared were these I (R3 = R4 = H, n = 2; R1, R2, and m.p. given): H, 4-ClC6H4, 185.2-6.8°; H, p-tolyl, 147.8-54.8°; 5-MeO, p-tolyl, 108.6-11.0°; H, PhCH:CHCH2, 258.2-63.6°. Also made was 1-[2-(3-indolyl)ethyl]-trans-2,5-dimethylpiperazine, m. 189.2-90.4°, and from VI and VII 1-[2-(3-indolyl)ethyl]-4-phenyl-3-piperazinone, m. 163.2-4.4°. Method B: To a cold solution of 79.2 g. 1-(o-tolyl)piperazine in 500 ml. tetrahydrofuran (VIII) was added 31.2 g. (3-indolyl)glyoxalyl chloride (IX), the white precipitate filtered off, the filtrate evaporated, the residual gum taken up in a warm mixture of 700 ml. H2O.

120 ml. AcOEt and 25 ml. AcOH, and the solid collected, to give 41.5 g. III (R1 = R3 = R4 = H, R2 = o-tolyl) (X). Similarly prepared were these III (R3 = R4 = H; R1, R2, and m.p. given): H, Me, --; H, HOCH2CH2, --; H, m-tolyl, --; H, 2-MeOC6H4, --; H, 4-MeOC6H4, 243-5°; H, 3,4-ClMeC6H3, 211-14°; 6-MeO, Ph, 205-9°; 6-MeO, o-tolyl, 247-50°; 6-MeO, m-tolyl, 206-8°; 6-MeO, p-tolyl, 196-8°; 6-MeO, 2-MeOC6H4, 246-8°; 6-MeO, 4-MeOC6H4, 205-10°; 5-PhCH2O, p-tolyl, 148-55°; 5-PhCH2O, PhCH2CH2, 135-40°; 5-MeS, Ph, 188-91°; 5-MeS, p-tolyl, 211-13°; 5,6-(CH2O2), Ph, 267-9°; 5,6-(CH2O2), o-tolyl, 214.6-15.8°; 5,6-(CH2O2), m-tolyl, 212-16°; 5,6-(CH2O2), p-tolyl, 266.4-78.4°; 5,6-(CH2O2), 2-MeOCH2CH2, 205-9°; 5,6-(MeO)2, Ph, 256.8-8.8°; 5,6-(MeO)2, o-tolyl, 211-16°; 5,6-(MeO)2, m-tolyl, 231-8°; 5,6-(MeO)2, p-tolyl, --; 5,6-(MeO)2, 2-MeOC6H4, 218-22°; 5,6-(MeO)2, 3-MeOC6H4, 234.4-6.4°; 5 6-(MeO)2, 4-MeOC6H4, 228-36°; 5,6-(MeO)2, 4-MeSC6H4, 236.4-8.2°; 5,6-(EtO)2, Ph, 180.0-1.0°; H, 2-pyridyl, 242-3°; 4-MeO, Ph, --; 5-MeO, Ph, 224-7.5°; 7-MeO, Ph, --; 6-Me, Ph, --; 6-EtO, Ph, 165° (decomposition); 6-MeO, 2-ClC6H4, 125.2-8.8°; 6-MeO, 3-ClC6H4, 214-16°; 6-MeO, 3-MeOC6H4, 211-13°; 6-MeO, 2-EtOC6H4, 180-4°; 6-MeO, 2,6-Me2C6H3, 215-18°; 6-MeO, 5,2-Cl(MeO)C6H3, 208-11°; 5,6-(MeO)2, PhCH2, 210.2-11.8°; 5,6-EtO(MeO), Ph, 215-22°; 5,6-(MeO)2, 2-pyridyl, 249.6-51.6°; 5,6-(OCH2CH2O), Ph, 172.5-8.5°; 5,6-(MeO)2, 2-EtOC6H4, 135-43°; 5,6-(MeO)2, 2,6-Me2C6H3, 253.2-6.2°; 5,6-(CH2O2), 4-MeOC6H4, 257-8°; 5,6-(CH2O2), 2-BuOC6H4, 164-7.5°; 5,6-(EtO)2, 2-MeOC6H4, 185-6.5°; 5,6-(EtO)2, 3-MeOC6H4, 162-5.5°; H, Ph, 224.2-5.6°; H, PhCH2, 174.4-5.6°; 5,6-(MeO)2, 2-ClC6H4, .apprx.214°; 6-Cl, Ph, 270-4°; 6-MeO, 2-pyridyl, 231-3°; 5,6-(MEO)2, 2-BuOC6H4, 171-4°; 5,6-(MeO)2, 2-EtC6H4, 193-8°; 5,6-(MeO)2, 2,5-(MeO)2C6H3, 208-10°; 5,6-(CH2O2), 2-pyridyl, 271-3°; 5,6-(MeO)2, 2-MeSC6H4, 219-21°. Also prepared were these III (R1, R2, R3, R4, and m.p. given): H, Ph, Me, H, --; 5,6-(MeO)2, Ph, Me, H, 163-74°; 5,6-(CH2O2), 4-MeOC6H4, Me, H, 173-266°; 5,6-(CH2O2), Ph, H, Me, 219-19.8°; 5,6-(MeO)2, Ph, H, Me, 215-22°; H, Ph, Me, Me, --; 6-MeO, Ph, Me, H, 218-20°; 6-MeO, Ph, Ph, H, 155-60°; 5,6-(MeO)2, 2-MeOC6H4, Me, H, 211.4-12.6°; 5,6-(MeO)2, o-tolyl, Me, H, 119-22°; 5,6-(MeO)2, m-tolyl, Me, H, 120-2°; 5,6-(MeO)2, 3-MeOC6H4, Me, H, 159-63.5°; 5,6-(CH2O2), 2-MeOC6H4, Me, H, 233-5°; 5,6-(MeO)2, Ph, Et, H, 177-84°; 5,6-(EtO)2, Ph, Me, H, 182-7°. A solution of 41.5 g. X in 250 ml. VIII was added to a suspension of 27 g. LiAlH4 in 300 ml. VIII, and the mixture refluxed 61/2 hrs. to give 28.5 g. I (R1, R3, R4 = H, R2 = o-tolyl, n = 2), m. 124.2-6.4°. Similarly prepared were these I (R3 = R4 = H, n = 2; R1, R2, and m.p. given): H, H, 149.8-52.0°; H, Me, -- (di-HCl salt m. 279.0-83.8°); H, HOCH2CH2, -- (di-HCl salt m. 266.8-71.4°); H, m-tolyl, 163.8-6.2°; H, 2-MeOC6H4, 111.4-14.2°; H, 4-MeOC6H4, 129.8-31.6°; H, 3,4-ClMeC6H3, 159.2-60.6°; 6-MeO, Ph, 137.4-9.6°; 6-MeO, o-tolyl, 139.2-41.4°; 6-MeO, m-tolyl, 119.8-23.4°; 6-MeO, p-tolyl, 172.2-3.4°; 6-MeO, 2-MeOC6H4, 98.2-100.2°; 6-MeO, 4-MeOC6H4, 185.6-8.6°; 5-PhCH2O, p-tolyl, 151.4-3.6°; 5-PhCH2O, PhCH2CH2, 121-3°; 5-MeS, Ph, 110.2-11.6°; 5-MeS, p-tolyl, 111-13.6°; 5,6-(CH2O2), Ph, 141.0-3.2°; 5,6-(CH2O2), o-tolyl, 159.2-60.8°; 5,6-(CH2O2), m-tolyl, 130.0-1.4°; 5,6-(CH2O2), p-tolyl, 187.0-8.8°; 5,6-(CH2O2), 2-MeOC6H4, 158.0-9.4°; 5,6-(MeO)2, Ph, 128.4-30.0°; 5,6-(MeO)2,

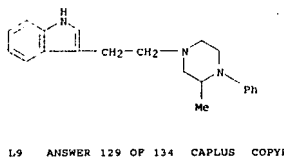
o-tolyl, -- (HCl salt m. 218.4-23.4°); 5,6-(MeO)2, m-tolyl, 118.4-19.6°; 5,6-(MeO)2, p-tolyl, 137.8-9.2°; 5,6-(MeO)2, 2-MeOC6H4, 116.0-16.6°; 5,6-(MeO)2, 3-MeOC6H4, 123.0-4.0°; 5,6-(MeO)2, 4-MeOC6H4, 158.8-64.0°; 5,6-(MeO)2, 4-MeSC6H4, 175.4-7.2°; 5,6-(EtO)2, Ph, 123.0-5.2°; H, 2-pyridyl, -- (HCl salt m. 232.2-4.4°); 4-MeO, Ph, 177.2-82.2°; 5-MeO, Ph, 147.4-50.0°; 7-MeO, Ph, 122.0-5.2°; 6-Me, Ph, 174.2-5.2°; 6-EtO, Ph, 159.6-63.2°; 6-MeO, 2-ClC6H4, 125.2-8.8°; 6-MeO, 3-ClC6H4, 103.6-4.4°; 6-MeO, 3-MeOC6H4, 142.0-4.6°; 6-MeO, 2-EtOC6H4, 159.4-61.4°; 6-MeO, 2,6-Me2C6H3, 135.2-6.8°; 6-MeO, 2,5-MeOC1C6H3, 121.8-8.6°; 5,6-(MeO)2, PhCH2 (XI), 113-14.4°; 5,6-EtO(MeO), Ph, 129.2-30.6°; 5,6-(MeO)2, 2-pyridyl -- (HCl salt m. 210.2-11.8°; 5,6-(OCH2CH2O), Ph, 170.8-6.8°; 5,6-(MeO)2, 2-EtOC6H4, 120.4-2.0°; 5,6-(MeO)2, 2,6-Me2C6H3, 117.8-19.6°; 5,6-(CH2O2), 4-MeOC6H4, 182.4-4.6°; 5,6-(CH2O2), 2-BuOC6H4, 125.0-6.4°; 5,6-(EtO)2, 2-MeOC6H4, 89.4-92.0°; 5,6-(EtO)2, 3-MeOC6H4, 97.6-8.4°; 6-Cl, Ph, 177.2-8.6°; 6-MeO, 2-pyridyl, 107.2-8.2°; 5,6-(MeO)2, 2-BuOC6H4, 93.8-5.8°; 5,6-(MeO)2, 2-EtC6H4, 104.2-7.2°; 5,6-(MeO)2, 2,5-(MeO)2C6H3, 136.8-7.8°; 5,6-(CH2O2), 2-pyridyl, -- (di-HCl salt m. 200-24°); 5,6-(MeO)2, 2-MeSC6H4, 116-17.8°. Also made were these I (n = 2; R1, R2, R3, R4, and m.p. given): H, Ph, Me, H, 154.2-5.6°; 5,6-(MeO)2, Ph, Me, H, -- (HCl salt m. 249.0-55.4°); 5,6-(CH2O2), 4-MeOC6H4, Me, H, 160.8-2.8°; 6-MeO, Ph, Me, H, -- (HCl salt m. 253.2-6.2°); 6-MeO, Ph, Ph, H, 148.2-8.8°; 5,6-(MeO)2, 2-MeOC6H4, Me, H, -- (di-HCl salt m. 217.4-20.8°); 5,6-(MeO)2, o-tolyl, Me, H, 119.8°-21.6°; 5,6-(MeO)2, m-tolyl, Me, H, -- (di-HCl salt m. 210.2-3.8°); 5,6-(MeO)2, 3-MeOC6H4, Me, H, -- (di-HCl salt m. 182.6-4.2°); 5,6-(CH2O2), 2-MeOC6H4, Me, H, 137.0-43.0°; 5,6-(CH2O2), 2-MeOC6H4, H, Me, 155.4-6.4°; 5,6-(MeO)2, Ph, Me, H, 139.6-40.4°; 5,6-(MeO)2, Ph, Et, H, --(HCl salt m. 237.6-9.0°); 5,6-(EtO)2, Ph, Me, H, 111.6-13.2°; 5,6-(CH2O2), 2-MeOC6H4, Me, Me, 118.2-19.6°; 5,6-(CH2O2), 2-MeOC6H4, Me, PhCH2, 169.2-70.2°; H, 2-MeOC6H4, H, Me, 74.6-6.4°. Catalytic debenzylation of XI gave I (R1 = 5,6-(MeO)2, R2, R3, R4 = H, n = 2), m. 109.6-11.4°, which reacted with 2-chloropyrimidine to give I (R1 = 5,6-(MeO)2, R2 = 2-pyrimidinyl, R3, R4 = H, n = 2), m. 127.2-8.2°. III (R4 = alkyl was reduced to II; other II were obtained as by-products in the LiAlH4 reduction of III. Thus were made these II (n = 1; R1, R2, R3, R4, and m.p. given): 5,6-(CH2O2), Ph, H, Me, 171-2.5°; 5,6-(MeO)2, Ph, H, Me, 128.4-30.2°; H, Ph, Me, Me, 136.8-9.6°; 5,6-(MeO)2, p-tolyl, H, H, 193.2-8.0°. Method C: On addition of 3-(4-benzhydryl-1-piperazinyl)propionyl chloride to a solution of 5-chloroindole and EtMgBr in ether, there was obtained IV (R1 = 5-Cl, R2 = Ph2CH, R3, R4 = H, n = 2) (XII), which with MeI and NaNH2 in liquid NH3 gave IV (R1 = 5-Cl, R2 = Ph2CH, R3 = H, R4 = Me, n = 2). Similarly made were these IV (R1, R2, R3,R4, and n given): H, Ph, Ph, H, 3; H, Ph, Ph, PhCH2, 3. XII was reduced by LiAlH4 to I (R1 = 5-Cl, R2 = Ph2CH, R3, R4 = H, n = 2), but XII reduced by NaBH4 yielded II (R1 = 5-Cl, R2= Ph2CH, R3 = R4 = H, n = 2). When IV (R4 = alkyl) was reduced by LiAlH4, then II was obtained. Thus were made these II (R1, R2, R3, R4 and n given): 5-Cl, Ph2CH, H, Me, 2; H, Ph, Ph, PhCH2, 3; 6-BuO, Me, H, 4-MeSC6H4CH2CH2, 3; 5,6,7-(MeO)3, Me, H, 4-BuOC6H4CH2CH2, 3; H, Me, H, 3-HOC6H4CH2CH2, 3; H, Me, H, PhCH:CHCH2, 3. Method D: To a cold solution of 22.5 g. 3-indoleacetic acid and 13.3 g. Et3N in 800 ml. Me2CO was added 18.1 g. ClCO2Bu-iso, the mixture stirred for 10 min. at -10°, a solution of 1-phenylpiperazine in little Me2CO added,

and the mixture kept 1.7 hrs. at room temperature to yield 5.4 g. V(R1, R2 = H, R3 = Ph, n = 1), m. 179.4-81.6°. Similarly prepared were these V (R3 = H; R1, R2, n, and m.p. given): H, Ph, 2, 136.2-7.4°; H, 3-MeOC6H4, 1, --; H, 2-ClC6H4, 2, --; H, o-tolyl, 2, --; H, 2-MeOC6H4, 2, 173.0-6.0°; H, Ph, 3, --; H, 2-MeOC6H4, 3, 129-32°; H, 3-MeOC6H4, 3, --; 6-MeO, Ph, 2, 169-72°; 6-MeO, 2-MeOC6H4, 2, 120.5-2.0°; 5,6-(MeO)2, 3-ClC6H4, 1, --; 5,6-(CH2O2), Ph, 2, 178-80°; 5,6-(MeO)2, 2-ClC6H4, 1, 185-8.5°; 5,6-(MeO)2, 2-MeOC6H4, 2, 124.8-7.4°; 5,6-(MeO)2, Ph, 2, 120.5-2.0°; 5,6-(MeO)2, 3-MeOC6H4, 2, --. Also obtained was V (R1 = 5,6-(MeO)2, R2 = Ph, R3 = Me, n = 2). Also made was 1-[3-(1-indolyl)propionyl]-4-phenylpiperazine, an oil and 1-[3-(2-methyl-5,6-dimethoxy-3-indolyl)propionyl]-4-phenylpiperazine. By reduction of these V by LiAlH4 in VIII were prepared these I (R3 = R4 = H; R1, R2, n, and m.p. given): H, Ph, 2, --; H, Ph, 3, 126.6-7.8°; H, 3-MeOC6H4, 2, 146.4-7.6°; H, 2-ClC6H4, 3, 140.3-3.6°; H, o-tolyl, 3, 102.4-4.2°; H, 2-MeOC6H4, 3, 156.8-9.2°; H, Ph, 4, 96.0-100.8°; H, 2-MeOC6H4, 4, 120.6-3.8°; H, 3-MeOC6H4, 4, -- (HCl salt, m. 234.2-5.8°); 6-MeO, Ph, 3, 196.4-7.6°; 6-MeO, 2-MeOC6H4, 3, 153.2-5.0°; 5,6-di-MeO, 3-ClC6H4, 2, --(HCl salt m. 236.8-9.2°); 5,6-(CH2O2), Ph, 3, 142.6-4.2°; 5,6-(MeO)2, 2-ClC6H4, 2, 86.8-9.8°; 5,6-(MeO)2, 2-MeOC6H4, 3, 120.4-1.4°; 5,6-(MeO)2, Ph, 3, 157.4-8.2°; 5,6-(MeO)2, 3-MeOC6H4, 3, 159.0-60.2°. Also made was I (R1 = 5,6-(MeO)2, R2= Ph, R3 = Me, R4 = H, n = 3), m. 117.8-18.8°, and 1-[3-(1-indolyl)propyl]-4-phenylpiperazine, m. 96.7-8.4°. Method E: A solution of 9.0 g. indole in 100 ml. dioxane was added to a cold solution of 6.25 ml. 40% aqueous CH2O and 13.3 g. 1-phenylpiperazine in 1 l. dioxane to give I (R1 = R3 = R4 = H, R2 = Ph, n = 1), m. 184.6-6.8°. Similarly made was I (R1 = 5,6-(MeO)2, R2 = Ph, R3 = R4 = H, n = 1), m. 159.3-60.2°. Method F: The piperazine ring was formed after a substituted ethylenediamine group had been joined to the indole moiety. Thus, 27 g. IX and 58 g. (PhCH2)NPhCH2CH2NH2 in 300 ml. VIII refluxed for 5 hrs. gave 41.9 g. N-benzyl-N-phenyl-N'-[(3-indolyl)glyoxalyl]ethylenediamine, m. 162.2-2.6°, which was reduced by LiAlH4 to N-benzyl-N-phenyl-N'-[2-(3-indolyl)ethyl]ethylenediamine (XIII) (di-HCl salt m. 171.4-5.4°). Also made were N-benzyl-N-methyl-N'-[(3-indolyl)glyoxalyl]ethylenediamine, m. 124.5-7.0°, and N-benzyl-N-methyl-N'-[2-(3-indolyl)ethyl]ethylenediamine, m. 102-5°. A solution of 11.1 g. XIII and 3.4 g. ClCH2COCl in CH2Cl2 was refluxed to yield 9.4 g. 4-[2-(3-indolyl)ethyl]-1-phenyl-1-benzyl-1m3-oxopiperazinium chloride, m. 157-9.5°, which was catalytically debenzylated to 1-[2-(3-indolyl)ethyl]-4-phenyl-2-piperazinone, m. 157.2-9.0°. Similarly made was 4-[2-(3-indolyl)ethyl]-1-methyl-1-benzyl-3-oxopiperazinium chloride, m. 229.5-32.5°, and 4-[2-(3-indolyl)ethyl]-2-methyl-1-phenyl-3-piperazinone, m. 186.4-91.8°. The latter, reduced by LiAlH4, gave 1-[2-(3-indolyl)ethyl]-3-methyl-4-phenylpiperazine, m. 116.2-17.6°.

IT 94961-31-6P, Indole, 3-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]-
RL: PREP (Preparation)
(preparation of)

RN 94961-31-6 CAPLUS

CN Indole, 3-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (7CI) (CA INDEX NAME)



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ACCESSION NUMBER: 1964:31020 CAPLUS
DOCUMENT NUMBER: 60:31020
ORIGINAL REFERENCE NO.: 60:5521f-h,5522a-h,5523a
TITLE: N-Phenylpiperazines
INVENTOR(S): Maxwell, Donald R.; Wragg, William R.
PATENT ASSIGNEE(S): May & Baker Ltd.
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PRIORITY APPLN. INFO.:			GB	19590320

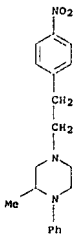
AB p-O2N C6H4CH2CH2Br (11.5 g.), 16.2 g. N-phenylpiperazine (I), and 150 cc. CHCl3 refluxed 24 hrs. gave Ia (R = p-O2NC6H4CH2CH2, R1 = H), m. 140-1° (CHC13-EtOH), which was hydrogenated over Pt.2 to give the p-amino analog; di-HCl salt (II) m. 314-17°. Treating the base of II with Ac2O gave the p-acetamido analog, m. 205-8°; isethionate m. 180-2°. Similarly were prepared the following Ia (R, R1, % yield, and m.p. given): p-AcNHC6H4CH2CH2, m-Cl, 57, 174-6°; p-O2NC6H4CH2CH2, o-Cl, 68, 108-10°; p-H2NC6H4CH2CH2, o-Cl, 52, - (di-HCl salt m. 306-9°); p-O2NC6H4CH2CH22, m-Cl, 59, 83-5°; p-H2NC6H4CH2CH2, m-Cl, 57, - (di-HCl salt m. 285-8°); p-O2NC6H4CH2CH2, p-Cl, 58, 147-9°; p-H2NC6H4CH2CH2, p-Cl, 61, - (di-HCl salt m. 319-22°); p-OHCNHC6H4CH2CH2, H, 100, 163-5° (HCl salt m. 255° (decomposition)); p-OHCNHC6H4CH2CH2, m-Cl (III), 67, 147-50°; p-OHCNMeC6H4CH2CH2, H, 95, 130-1°. An alc. solution of di-p-Me2NC6H4CH2CHMeNH2 (IV) and PhN(CH2CH2Br)2 was refluxed 5.5 hrs., the mixture cooled, treated with Na2CO3, and refluxed 6 hrs. to give 32% dl-Ia (R = p-Me2NC6H4CH2CHMe, R1 = H), m. 114-15°. IV.2HCl, m. 213-16°, was obtained by LiAlH4 reduction of p-dimethylamino β-methyl-β-nitrostyrene, m. 120-1°, obtained in 79% yield by condensing p-Me2NC6H4CHO with EtNO2 in C6H6. II and ClCO2Me in CHCl3 gave 77% Ia (R = p-MeO2CNHC6H4CH2CH2, R1 = H), m. 158-9°. Prepared also was 39% Ia (R = p-MeO2CNHC6H4CH2CH2, R1 = o-Cl), m. 124-5°, 98% Ia.HCl (R = p-ClCH2CH2O2CNHC6H4CH2CH2, R1 = H) (V), m. 256° (decomposition) (free base m. 133-5°), and 76% Ia. HCl (R = p-ClCH2CH2O2CNHC6H4CH2CH2, R1 = o-Cl) (VI), m. 233-5°. Addition of Br in glacial HOAc to p-H2NC6H4CH2CH2Br. HCl gave 78% 2-(4-amino-3,5-dibromophenyl)ethyl bromide, m. 96-9°, which was refluxed with I to give 47% 1-[2-(4-amino-3,5-dibromophenyl)ethyl]4-phenylpiperazine, m. 106-7°. Refluxing V with alc. KOH gave 14% 3-[4-[2-(4-phenylpiperazinyl)ethyl]phenyl]oxazolid-2-one, m. 194-6°. Refluxing VI with alc. KOH gave 77% Ia (R = p-HOCH2CH2NHC6H4CH2CH2, R1 =

o-Cl), m. 113-14°. Ia (R = p-H2NCONHC6H4CH2CH2, R1 = H), m. 315-18°, was obtained in 42% yield by refluxing an aqueous solution of NaCNO and II. Refluxing p-nitrostyrene bromohydrin and I in toluene gave 57% dl-Ia (R = p-O2NC6H4CH(OH)CH2, R1 = H), m. 167-8°, reduced catalytically to 80% the amino analog, m. 144-5 °. I and p-MeO3SNHC6H4CH2CH2Br, m. 104-5°, from MeO3SCl and p-aminophenethyl bromide, was refluxed to give 63% Ia (R = p-MeO3SNHC6H4CH2CH2, R1 = H), m. 153-5°. III in tetrahydrofuran was added to LiAlH4, and the mixture refluxed to give 83% Ia (R = p-MeNHC6H4CH2CH2, R1 = m-Cl), m. 96-8°. Refluxing I and p-F3CCONHC6H4CH2CH2Br, m. 107-11°, from p-H2NC6H4CH2CH2Br and trifluoroacetic anhydride, gave 40% Ia (R = p-F3CCONHC6H4CH2CH2, R1 = H), m. 170-2°. p-FC5H4NH2 and diethanolamine was treated with HBr, the mixture heated to 180-90°, and H2O distilled to give 30% N-p-fluorophenylpiperazine, b0.1 118-23°, which was converted into Ia (R = p-O2NC6H4CH2CH2, R1 = p-F), m. 127-9°. This, when hydrogenated, gave 57% the amino analog; HCl salt m. 280-4°. Prepared similarly were 47% N-m-fluorophenylpiperazine-HBr, m. 232-5°, 54% Ia (R = p-O2NC6H4CH2CH2, R1 = m-F), m. 118-20°, and 62% the p-H2N analog as HCl salt, m. 282-5°. Ethylene oxide was treated with m-anisidine to give N,N-bis(β-hydroxyethyl)m-anisidine, which was treated with POCl3 to give 74% N,N-bis(β-chloroethyl)-m-anisidine as an oil. This when added to a mixture of p-nitrophenethylamine-HCl and anhydrous Na2CO3 in BuOH and refluxed gave 54% Ia (R = p-O2NC6H4CH2CH2, R1 = m-MeO), m. 118-20°, which was hydrogenated to give 67% the p-amino analog as HCl salt, m. 255-8°. Similarly prepared were 77% N,N-bis(β-hydroxyethyl)-o-fluoroaniline, b4 141-7°, 95% N,N-bis(β-chloroethyl)-o-fluoroaniline, 62% Ia (R = p-O2NC6H4CH2CH2, R1 = o-F), m. 118-20°, Ia. HCl (R = p-H2NC6H4CH2CH2, R1 = o-F), m. 239-41°, 48% N-m-bromophenylpiperazine-HBr, m. 215-18°, 65% Ia (R = p-O2NC6H4CH2CH2, R1 = m-Br), m. 238-41°, Ia.2HCl (R = p-H2NC6H4CH2CH2, R1 = m-Br), m. 256-9°, 69% Ia (R = p-O2NC6H4CH2CH2R1 = o-Me), m. 103-3°, 73% Ia.2HCl(R = p-H2NC6H4CH2CH2, R1 = o-Me), m. 315-17°, 57% Ia (R = p-O2NC6H4CH2CH2, R1 m-Me), m. 115-17°, 66% Ia.2HCl (R = p-H2NC6H4CH2CH2, R1 = m-Me), m. 303-5°, 30% N-(2-methyl-5-chlorophenyl)piperazine-HBr, m. 265-7°, 36% Ia (R = p-O2NC6H4CH2CH2, R1 = 2,5-MeCl), m. 87-8°, 60% Ia.2HCl (R = p-H2NC6H4CH2CH2, R1 = 2,5-MeCl), m. 325-7°, 52% N-(3,5-dichlorophenyl)piperazine-HBr, m. 309-13°, 58% Ia (R = p-O2NC6H4CH2CH2, R1 = 3,5-Cl2), m. 92-4°, 56% Ia (R =p-H2NC6H4CH2CH2, R1 = 3,5-Cl2), m. 91-2°, 42% N,N-bis(β-hydroxyethyl)-2,3-dichloroaniline, b0.08 170-82°deg., 52% Ia (R = p-O2NC6H4CH2CH2, R1 = 2,3-Cl2), m. 145-7°, 55% Ia.HCl (R = p-H2NC6H4CH2CH2, R1 = 2,3-Cl2), m. 241-3°, 21% N-(3,4-dichlorophenyl)piperazine, b15 202°, 67% Ia (R = p-O2NC6H4CH2CH2, R1 = 3,4-Cl2), m. 119-20°, 57% Ia.3HCl (R = p-H2NC6H4CH2CH2, R1 = 3,4-Cl2), m. 326-8°, 47% dl-1-[2-(p-nitrophenyl)ethyl]-3-methyl-4-phenylpiperazine, m. 108°, 39% dl-1-[2-(p-aminophenyl)ethyl]-3-methyl-4-phenylpiperazine-HCl, m. 265-9°, 34% Ia (R = p-O2NC6H4CH2CH:CHCH2, R1 = H), m. 117-18°, 28% Ia. HCl [R = p-H2NC6H4(CH2)4, R1 = H], m. 275-8°, 4-(2-chloro-4-nitrophenyl)but-2-enyl chloride, m. 47-8°, Ia (R = 2,4-Cl(O2N)C6H3CH2CH:CHCH2, R1 = H], m. 94-5°, 35% 2-(4-methoxy-3-nitrophenyl)ethyl bromide, m. 52-3°, 68% Ia [R = 3,4-(O2N)(MeO)C6H3CH2CH2, R1 = H], m. 106-7°, 65% Ia [R = 3,4-(H2N)(MeO)C6H3CH2CH2, R1 = H], m. 147-8°, 61% Ia.HCl (R = p-H2NC6H4CH2CH:CHCH2, R1 = H), m. 246-7°, Ia. HCl [R = 2,4-Cl(H2N)C6H3CH2CH:CHCH2, R1 = H], m. 228-31°, 54% 4-chloro-p-acetamidobutyrophenone, m. 162-4°,

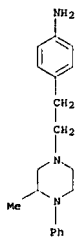
13% Ia (R = p-AcNHC6H4CO(CH2)3, R1 = H), m. 172-4°, 63% 4-(m-nitro-p-fluorophenyl)-4-oxobutyl chloride, m. 63-4°, Ia [R = 4,3-F(O2N)C6H3CO(CH2)3, R1 = H], m. 110-12°, 16% Ia [R = 4,3-F(H2N)C6H3CO(CH2)3, R1 = H], m. 147-50°, 76%, dl-N(β-hydroxyethyl)-N-(β-hydroxypropyl)aniline, b0.15 135-42° 26%, dl-1-[2-(p-nitrophenyl)ethyl]-2-methyl-4-phenylpiperazine', m. 82-4°, and 75% dl-1-[2-(p-aminophenyl)ethyl]-2-methyl- 4-phenylpiperazine-HCl, m. 247-50°. These compds. had pharmacological and psychotropic properties.

IT 94915-72-7P, Piperazine, 2-methyl-4-(p-nitrophenethyl)-1-phenyl- 100175-11-9P, Piperazine, 4-(p-aminophenethyl)-2-methyl-1-phenyl-, hydrochloride
RL: PREP (Preparation)
(preparation of)

RN 94915-72-7 CAPLUS
CN Piperazine, 2-methyl-4-(p-nitrophenethyl)-1-phenyl- (7CI) (CA INDEX NAME)



RN 100175-11-9 CAPLUS
CN Piperazine, 4-(p-aminophenethyl)-2-methyl-1-phenyl-, hydrochloride (7CI) (CA INDEX NAME)



●x HCl

L9 ANSWER 130 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:9840 CAPLUS
DOCUMENT NUMBER: 60:9840
ORIGINAL REFERENCE NO.: 60:1774f-h
TITLE: Piperazines
INVENTOR(S): Stevens, George de; Mull, Robert P.
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 31 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 615259		19620919	BE	<--
FR 1332560			FR	
GB 995036			GB	
PRIORITY APPLN. INFO.:			US	19610320

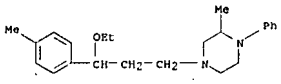
GI For diagram(s), see printed CA Issue.

AB The title compds. (I) and their salts are valuable pharmaceuticals, especially vasodilators and diagnostic agents of low toxicity. They have adrenolytic properties. 2-Methyl-1-phenylpiperazine (8.8 g.) was dissolved in 50 cc. PhMe, 2.4 g. 53% suspension of NaH in mineral oil added, the mixture refluxed 2 hrs., 11.6 g. 5-ethoxy-3-(4-methylphenyl)propyl chloride added, the mixture refluxed overnight and filtered, and the filtrate evaporated in vacuo and distilled to give I (Ar = 4-MeC6H4, R = Et, R1 = Me, X = Ph), b0.2 182-4°; di-HCl salt m. 190-2° (EtOH). Similarly, the following I were prepared (Ar, R, R1, X, b.p./mm., and m.p. of di-HCl salt given): Ph, Et, Me, Ph, 168-70°/0.075, 194°; 4-ClC6H4, Et, Me, Ph, 210-15°/0.27, 174-6°; 4-ClC6H4, Me, Me, Ph, 170?°/0.05, 184°; 4-MeC6H4, iso-Pr, Me, Ph, 146-54°/0.04 169°; Ph, Et, H, Ph, 160°/0.15, 202-3° (EtOH-Et2O); 4-ClC6H4, Me, H, Ph, 178-80°/0.1,212-

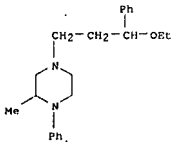
13°; 4-ClC6H4, Et, H, Ph, 168°/0.1, 208°; 4-MeC6H4, Et, H, 2-pyridyl, 162-3°/0.25, - (triHCl salt m. 194-5°).

IT 442-26-2P, Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 745-60-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl- 748-03-8P, Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 905-92-0P, Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl- 907-68-6P, Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride 978-11-0P, Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl-, dihydrochloride 1051-75-8P, Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl- 1051-76-9P, Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl-, dihydrochloride 1168-17-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride 3792-38-9P, Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

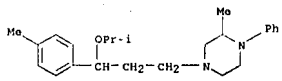
RN 442-26-2 CAPLUS
CN Piperazine, 4-[3-ethoxy-3-(4-methylphenyl)propyl]-2-methyl-1-phenyl- (9CI) (CA INDEX NAME)



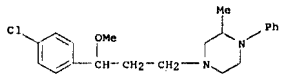
RN 745-60-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



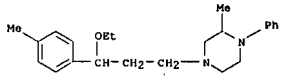
RN 748-03-8 CAPLUS
CN Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 905-92-0 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl- (8CI) (CA INDEX NAME)

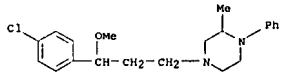


RN 907-68-6 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



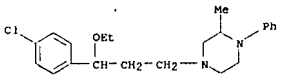
●2 HCl

RN 978-11-0 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

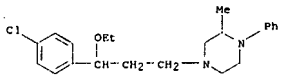


●2 HCl

RN 1051-75-8 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)

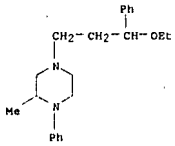


RN 1051-76-9 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



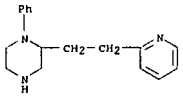
●2 HCl

RN 1168-17-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

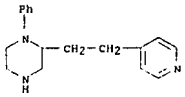


●2 HCl

RN 3792-38-9 CAPLUS
CN Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



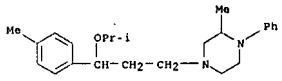
RN 97018-75-2 CAPLUS
CN Piperazine, 1-phenyl-2-[2-(4-pyridyl)ethyl]- (7CI) (CA INDEX NAME)



L9 ANSWER 132 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:6735 CAPLUS
DOCUMENT NUMBER: 58:6735
ORIGINAL REFERENCE NO.: 58:1086c-e
TITLE: Two-component diazotype layers
PATENT ASSIGNEE(S): Kalle A.-G.
SOURCE: 9 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 611215		19620606	BE	<--
DE 1226878			DE	
GB 955886			GB	
US 3139341		19640630	US 1961-156117	19611130 <--

PRIORITY APPLN. INFO.: DE 19601209
AB The preparation of a two-component diazotype material containing in the light-sensitive layer a piperazine derivative of the general structure I, where R and R' are lower alkyl groups and R'' is an alkyl, aralkyl, aryl, CO2H, or carbalkoxy group, and a diazonium salt is described. A solution of MeOCH2CH2OH 45, MeCOEt 45, H2O 10 parts, citric acid 1.5, B(OH)3 1.6 parts, sulfosalicylic acid 0.6 parts, 3,5-dimethyl-2-(4-methyl-1-piperazinylmethyl)phenol, m. 99-100°, 4.5 and [3,4-Me(EtNH)C6H3N2]BF4 4.0 parts coated onto a cellulose acetate film, and the dried film exposed under a transparency to the light of a 12-amp. arc and developed in the usual manner with NH3 vapor gave a yellow transparency of the original suitable for further reproduction.
IT 99750-96-6, Mesitol, α4-(3-methyl-4-phenyl-1-piperazinyl)-, hydrochloride
(in diazotype process)
RN 99750-96-6 CAPLUS
CN Mesitol, α4-(3-methyl-4-phenyl-1-piperazinyl)-, hydrochloride (7CI)



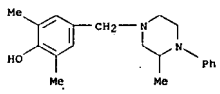
●2 HCl

L9 ANSWER 131 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:462412 CAPLUS
DOCUMENT NUMBER: 59:62412
ORIGINAL REFERENCE NO.: 59:11521a-c
TITLE: N-Aryl-N'-(2-pyridylethyl)piperazines
INVENTOR(S): Boissier, Jacques R.; Ratouis, Roger
PATENT ASSIGNEE(S): Societe Industrielle pour la Fabrication des Antibiotiques (S.I.F.A.)
SOURCE: 11 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR M1769		19630506	FR	<--

PRIORITY APPLN. INFO.: GB 19610317
OTHER SOURCE(S): MARPAT 59:62412
AB N-Arylpiperazines are treated with vinylpyridines in the presence of hydroquinone or tert-butyl-pyrocatechol (I) to give the title compds. which can be used in the treatment of hypertension. Thus, a mixture of 10.5 g. 2-vinyl-pyridine, 18 g. N-phenylpiperazine, and 10 mg. I is heated at 150° for 2 hrs., cooled, the unreacted starting materials distilled under 0.05-0.2 mm. at a bath temperature of 180-200°, and the residue re-crystallized in 400 ml. petr. ether to give 14 g. N-[2-(2-pyridyl)-ethyl]-N'-phenylpiperazine, m. 58°, 53% yield. Similarly prepared are (m.p. given): N-[2-(4-pyridyl)ethyl]-N'-phenyl-piperazine, 83° (petr. ether); N-[2-(2-pyridyl)ethyl]-N'-(2-pyridyl)piperazine, 69° (heptane); N-[2-(4-pyridyl)ethyl]-N-(2-pyridyl)piperazine, 82° (60% aqueous EtOH); N-[2-(2-pyridyl) ethyl]-N'-(2-chlorophenyl)piperazine, 64° (heptane), N-[2-pyridyl)ethyl]-N'-(2-chlorophenyl)piperazine, 69° (hexane); N-[2-(2-pyridyl)ethyl]-N'-(2-methoxyphenyl)piperazine, 47° (hexane); N-[2-(4-pyridyl)ethyl]-N'-(2-methoxyphenyl)-piperazine, 98° (heptane); N-[2-(4-pyridyl)ethyl]-N'-(2-bromo- phenyl)piperazine, 73° (hexane); N-[2-(4-pyridyl)ethyl]-N'-(2-ethoxyphenyl)piperazine, 66° (heptane); and N-[2-(4-pyridyl)-ethyl]-N'-(2-methylphenyl)piperazine, 68°.
IT 97018-74-1P, Piperazine, 1-phenyl-2-[2-(2-pyridyl)ethyl]-
97018-75-2P, Piperazine, 1-phenyl-2-[2-(4-pyridyl)ethyl]-
RL: PREP (Preparation)
(preparation of)
RN 97018-74-1 CAPLUS
CN Piperazine, 1-phenyl-2-[2-(2-pyridyl)ethyl]- (7CI) (CA INDEX NAME)

(CA INDEX NAME)



●x HCl

L9 ANSWER 133 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1961:28013 CAPLUS
DOCUMENT NUMBER: 55:28013
ORIGINAL REFERENCE NO.: 55:5549c-i,5550a-i,5551a-g
TITLE: 1-Arylalkyl-4-arylpiperazines
INVENTOR(S): Janssen, Paul A. J.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 589092		19600415	BE	<--
DE 1185615			DE	
GB 872352			GB	

AB 1-(γ-Benzoylpropyl)-4-phenylpiperazine, m. 89-90° (6:5 iso-PrOH-H2O), was prepared by reaction of 7.5 g. chlorobutyrophenone and 13.4 g. 1-phenylpiperazine 6 hrs. at room temperature and 4 hrs. at 105-10°; after cooling, 200 g. Et2O was added, the solution dried and evaporated, the residue dissolved in hot 4:1 70% EtOH-Et2O, and precipitated on cooling. The following 1-(arylalkyl)piperazines (1-arylalkyl = γ-benzoylpropyl) were thus prepd (4-aryl group and m.p. given): 3-fluorophenyl, 80.2-1.6° (iso-Pr2O); 3-chlorophenyl, 88-90°; 4-chlorophenyl, 127-8° (10:1 petr. ether-EtOH); 2-tolyl (HCl salt), 205-7° (5:4:3 iso-PrOH-MeOH-acetone); 3-tolyl, 78-9° (13:1 petr. ether-EtOH); 4-tolyl, 87.5-8.5° (iso-PrOH-H2O); 2,5-xylyl (HCl salt), 229-30°; 2-anisyl (di-HCl salt), 207.5-9.5° (iso-PrOH); 4-anisyl, 85-6° (iso-Pr2O); 2-pyridyl, 63-4.8°; 6-methyl-2-pyridyl, 72-5.8°; 4-methyl-2-pyridyl, 65.5-6.5°; 3-cyano-2-pyridyl, 45.5-7°; 5-methyl-2-pyridyl, 71.5-3°; 2-pyrimidyl, 78-9°; 4-methyl-2-pyrimidyl, 62.4-3.2°; 4,6-dimethyl-2-pyrimidyl, 97.4-8°. The following 1-(δ-benzoylbutyl)piperazines: Ph (di-HCl salt), 209-12° (8:8:1 acetone-iso-PrOH-MeOH); 3-tolyl (di-HCl salt), 191.5-2.5°; 2-pyridyl (di-HCl salt), 206.5-7.5°. 1-[γ-(4-Fluorobenzoyl)propyl]piperazines: Ph, 104-6° (iso-PrOH); 3-fluorophenyl (di-HCl salt), 198-200°; 4-fluorophenyl (di-HCl salt), 199.5-201.1°; 4-fluorophenyl (HCl salt), 180.2-1.6° (acetone-iso-PrOH); 3-chlorophenyl (HCl salt), 211-14° (iso-PrOH); 3-chlorophenyl (HCl salt), 197.8-9.5° (acetone-MeOH); 4-chlorophenyl, 96-8° (40:3 petr. ether-EtOH); 2-tolyl (HCl salt), 238-41° (decomposition); 3-tolyl (di-HCl salt),

210-13° (decomposition); 4-tolyl, 99-101° (iso-PrOH-H2O); 2,5-xylyl (di-HCl salt), 237.5-9.5°; 2-anisyl, 67.5-8.5° (iso-Pr2O) (di-HCl salt m. 205-5.5°); 4-anisyl, 104.6-5.5° (iso-PrOH), 5-methyl-2-pyridyl, 92-3°; 4-methyl-2-pyrimidyl (di-HCl salt), 215-20°. 1-[γ-(4-Chlorobenzoyl)propyl]piperazines: Ph, 113.5-14.5°; 3-chlorophenyl, 86-8°; 3-tolyl, 99.6-110.4°; 4-tolyl, 129.5-30.5°; 4-anisyl, 126.6-7.8°), 4-fluorophenyl (HCl salt), 207-9°; 4-chlorophenyl, 127-8.5°; 2-pyridyl, 82.5-4.4°. 1-[γ-(4-Methylbenzoyl)propyl]piperazines: Ph, 103-4.8°; 2-chlorophenyl, 106-7°, 3-chlorophenyl, 124.5-5.5°; 4-chlorophenyl, 134.5-6°; 3-tolyl, 87-8.5°; 4-tolyl, m. 117.2-19.2°, 2-pyridyl, 92-3°; 4-anisyl, 123.2-4°. 1-[γ-(2,5-Dimethylbenzoyl)propyl]piperazines: Ph (HCl salt), 179.5-80.5°. 1-[γ-(4-Anisoyl)propyl]piperazines: 3-fluorophenyl, m. 111-13°; 2-chlorophenyl, 73.5-3.8°; 3-iodophenyl, -; 3-chlorophenyl, 101.6-2.4°; 4-chlorophenyl, 128.6-30°; 2-tolyl (HCl salt), 239.5-40.5°; 3-tolyl, 105-6°; 4-tolyl, 126.6-7.6°; 2,5-xylyl (HCl salt), 225-6°; 2-anisyl (di-HCl salt), 197-8.2°; 4-anisyl, 125.6-7.4°. 1-[γ-(2,4-Dimethoxybenzoyl)propyl]piperazines: Ph (di-HCl salt), 195-6°; 2-tolyl (HCl salt), 177-9.2°; 2-anisyl (HCl salt), 214-15°; 2-pyridyl, 84.5-5.5°; 4-methyl-2-pyridyl, 79-80.8°. 1-[γ-(3,4-Dimethoxybenzoyl)propyl]piperazines: Ph, 101-3.5°; 2-pyridyl, 104.5-6.9°; 4-methyl-2-pyridyl, 85.4-6.5°. 1-[γ-(2,5-Dimethoxybenzoyl)propyl]piperazines: Ph(di-HCl salt), 179-80°. 1-[γ-(2,3,4-Trimethoxybenzoyl)propyl]piperazines: Ph, 113-16.2°. 1-[γ-(4-Ethoxybenzoyl)propyl]piperazines: Ph, 125.2-6.8°; 3-tolyl, 113.4-13.8°. 1-(β-Methyl-γ-benzoylpropyl)piperazines: Ph (di-HCl salt), 219.5-21.5°; 3-tolyl, 82.8-3.8° (petr. ether); 2-anisyl (di-HCl salt), 193-7°. 1-[γ-(4-Iodobenzoyl)propyl]piperazines: 5-methyl-2-pyridyl, -; 2-pyridyl, -; 4-methyl-2-pyrimidyl (di-HCl salt), -; 2-thiazolyl, -. 1-[γ-(4-Methoxybenzoyl)propyl]piperazines: 6-methyl-2-pyridyl, 74.6°; 4-methyl-2-pyridyl, 69.5-70.5°; 5-methyl-2-pyridyl, 84.6-6°; 3-cyano-2-pyridyl, 73.5-5.5°; 2-pyrimidyl, 83-3.5°; 2-thiazolyl (di-HCl salt), 122-4°; 4-methyl-2-pyrimidyl, 90°; 4,6-dimethyl-2-pyrimidyl, 71.8-4.2°; 2-(4-methyl)thiazolyl, 62.5-72° (di-HCl salt m. 187-201°); 2-(5-methyl-1,3,4-thiadiazolyl), 111.5-12.5°. 1-[γ-(2-Thenoyl)propyl]piperazines: 2-pyridyl, 70-1°; 5-methyl-2-pyridyl, 89.5-90.5°; 4-methyl-2-pyridyl, 65-6°; 6-methyl-2-pyridyl, 107.5-8.5°; 3-cyano-2-pyridyl, 71.5-2.5°; 2-pyrimidyl, 57.5-8.6°; 4-methyl-2-pyrimidyl, 52-3° (di-HCl salt m. 214.8-17°); 4,6-dimethyl-2-pyrimidyl, 64.5-5.6°; 2-thiazolyl, 52.2-4.6°; 2-(4-methyl)thiazolyl (di-HCl salt), 163-6°; 2-(5-methyl-1,3,4-thiadiazolyl), 83.6-5.6°, Ph (HCl salt), 186-7°; 3-fluorophenyl, 68.2-70.2°; 2-chlorophenyl (HCl salt), 202.5-3°; 3-chlorophenyl, 103.6-4.6°; 4-chlorophenyl, 94.5-6.5°; 2-tolyl (HCl salt), 212-13°; 3-tolyl, 74-6°; 4-tolyl, 77.5-8.5°; 2,5-xylyl (di-HCl salt), 214-15°; 2-anisyl (di-HCl salt), 197-201.8°; 4-anisyl, 69-70°. 1-[γ-(4-Fluorobenzoyl)propyl]piperazines: 4,6-dimethyl-2-pyrimidyl, 85.5-7.5°; 2-pyrimidyl, 111.6-12.8°; 2-thiazolyl, 74.5-6.5°; 2-(5-methylthiazolyl), 73-5.2°, 2-(5-methyl-1,3,4-thiadiazolyl), 105-6°, 2-(1,3,4-thiadiazolyl), 94.6-5.8°. 1-(γ-Benzoylpropyl)piperazines: 2-thiazolyl,

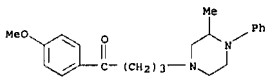
61.5-4°; 2-(4-methylthiazolyl)(di-HCl salt), 186-8°; 2-(1,3,4-thiadiazolyl), 59-64°; 2-(5-methyl-1,3,4-thiadiazolyl), 98-100.2°. 1-(γ-Benzoylpropyl)-4-(4-fluorophenyl)piperazine di-HCl salt, m. 214.5-17° (1:2:2 acetone-iso-PrOH-MeOH), was prepared by heating in a sealed tube 72 hrs. at 145-50° 9.1 g. γ-chlorobutyrophenone, 23 g. 1-(4-fluorophenyl)piperazine, and 0.1 g. KI, extracting the cooled mixture with H2O and Et2O, and treating the dried organic layer with dry HCl; the base was liberated in aqueous alkaline solution, m. 104-5.5° (EtOH). 1-[γ-(4-Anisoyl)propyl]-4-phenylpiperazine, m. 126.6-7.5°, and the corresponding 4-fluorophenyl derivative, m. 121.2-1.8°, 1-[γ-(2-thenoyl)propyl]-4-phenylpiperazine-2HCl, decomposed at 203-5°, and the 4-fluorophenyl analog, m. 82.5-3°, were similarly prepared 1-[γ-(4-Fluorobenzoyl)propyl]-4-(3-methyl-2-pyridyl)piperazine-HCl, m. 212-20° (iso-Pr2O), was prepared from 4.4 g. γ-chloro-4-fluorobutyrophenone and 7.8 g. 1-(3-methyl-2-pyridyl)piperazine in 120 cc. C6H6 in a sealed tube at 125° 24 hrs. The following derivs. were similarly prepared 1-[γ-(4-Fluorobenzoyl)propyl] compound (4-aryl and m.p. given): 4-methyl-2-pyridyl, 79.5-81°; 3-cyano-2-pyridyl, 71.5-3.5°; 6-chloro-3-pyridazinyl, 152-3.9°. 1-[γ-(4-Methoxybenzoyl)propyl] compound: 6-chloro-3-pyridazinyl, 176-6.8°. 1-[γ-(2-Thenoyl)propyl] compound: 6-chloro-3-pyridazinyl, 138-8.8°; 6-methoxy-3-pyridazinyl, 98.8-9.8°. 1-(γ-Benzoylpropyl)-4-benzoylpiperazine, m. 85-6° (iso-Pr2O), was prepared by heating a stirred mixture of 7 g. 1-(γ-benzoylpropyl)piperazine, 60 g. C6H6, 50 g. 10% NaOH solution, and (dropwise) 4.5 g. BzCl, and keeping the mixture at 70° 45-60 min. The following 1-(γ-benzoylpropyl) compds. were similarly prepared (same data): 4-fluorobenzoyl (HCl salt), 214.5-16.5°; 2-chlorobenzoyl (HCl salt), 216-17.5°; 3-chlorobenzoyl (HCl salt), 210.5-12.5°; 4-chlorobenzoyl, 98-9°; 3-trifluoromethylbenzoyl, 77.5-9°; 2-anisoyl (HCl salt), 140.8-3°; 2,6-dimethoxybenzoyl (oxalate); 193.1-4.8°; 3,4,5-trimethoxybenzoyl (oxalate), 187.4-8.2°; 5-(3-methyl-1,2,4-thiadiazolyl), 78-9°; 3-carboxamido-2-pyridyl, 112.6-14.2°. 1-[γ-(4-Fluorobenzoyl)propyl] compds.: benzoyl (HCl salt), 228-32.5°. 1-[γ-(4-Anisoyl)propyl] compds.: benzoyl (HCl salt), 200.2-3.2°; 4-fluorobenzoyl, 65.2-6.2°; 2-anisoyl, 97-8.2°; 2,6-dimethoxybenzoyl (oxalate), 201.5-1.8°. 1-[γ-(2-Thenoyl)propyl] compds.: 4-fluorobenzoyl, 82.5-3.5°; 4-nicotinoyl, 64.6-5.8°; 2-thenoyl, 85.6-7.4°. 1-Phenyl-4-[4-phenylpiperazinyl)-1-butanol-2-HCl, m. 198-200°, was prepared by reaction of 8.5 g. 1-(γ-benzoylpropyl)-4-phenylpiperazine and 0.25 g. NaBH4 in 160 cc. absolute EtOH 2 hrs. at 45° and decomposition with 2N HCl; the distillation residue was treated with aqueous alkali solution, extracted with Et2O, and treated with dry HCl. Following 1-phenyl-4-(R-substituted-piperazinyl)-1-butanols were similarly prepared (R given); 4-(3-tolyl), 83.5-4.5°; 4-(4-tolyl), 90.2-1.8°; 4-(3-fluorophenyl), 70-1.5°; 4-(3-chlorophenyl), 99-9.9°; 4-(4-chlorophenyl), 105-6°; 4-(4-anisyl), 91.5-2.6°; 4-(4-methyl-2-pyrimidyl), 78.5-80°; 4-(2-pyridyl), 113.8-14.8°. 1-(4-Tolyl) analogs: 4-Ph, 104-5.6°; 4-(4-tolyl), 105-6°; 4-(4-anisyl), 84-5°; 4-(2-pyridyl), 119.2-19.8°. 1-(2,5-Xylyl) analogs: 4-Ph, 92.8-3.8°. 1-(4-Fluorophenyl) analogs: 4-Ph, 85.5-7.5° (HCl salt m. 143.5-6.5°); 4-(3-chlorophenyl), 100-1.8°; 4-(4-chlorophenyl), 112.5-13.8°; 4-(2-anisyl), 105-6°; 4-(4-tolyl), 93-5°; 4-(2-pyridyl), 104-5°. (4-Chlorophenyl)

analogs: 4-Ph, 93.5-5°; 4-(3-chlorophenyl), 84-5°; 4-(4-chlorophenyl), 132-3°; 4-(3-tolyl), 93-4.5°. 1-(4-Anisyl) analogs: 4-Ph, 104.2-7.2°; 4-(2-chlorophenyl), 106.8-8.4°; 4-(3-tolyl), 119.5-21.5°; 4-(4-tolyl), 109.5-10.2°. 1-(4-Ethoxyphenyl) analogs: 4-Ph, 113-14.8°. 1-(2-Thienyl) analogs: 4-Ph, 91.4-3°; 4-(3-tolyl), 76-8°; 4-(4-tolyl), 113-14°; 4-(3-fluorophenyl), 78-9°; 4-(4-chlorophenyl), 109.2-10°; 4-(2-chlorophenyl), 85.5-7.5°; 4-(3-chlorophenyl), 81.5°; 4-(2-pyridyl), 95-7°; 4-(2-pyrimidyl), 97.6-9.4°. 1-Phenyl-5-(4-phenylpiperazinyl)-1-pentanol, m. 111-12°, and 1-phenyl-5-[4-(3-tolyl)piperazinyl]-1-pentanol, m. 107.4-9.2°, were also prepared 1-[γ-(4-Anisoyl)propyl]-4-(6-methyl-2-pyridyl)piperazine, m. 74-6°, was prepared by heating 8 hrs. at 110° 6.2 g. γ-chloro-4-methoxybutyrophenone and 8.9 g. 1-(6-methyl-2-pyridyl)piperazine. 1-(γ-Benzoylpropyl)-4-(6-methylthio-3-pyridazinyl)piperazine, m. 124-5°, was prepared by heating in a sealed tube 48 hrs. at 140-50°, 14.8 g. 1-(γ-benzoylpropyl)piperazine, 5 g. 3-chloro-6-(methylthio)pyridazine, 120 g. toluene, and 0.01 g. KI. N-(4-Tolylsulfonyl)-N-(β-hydroxyethyl)-N-(β-hydroxypropyl)amine (I), m. 66.2-8.2° (iso-PrOH and petr. ether at -20°), was prepared by adding 190.5 g. 4-toluenesulfonyl chloride to 119 g. N-(β-hydroxyethyl)-N-(β-hydroxypropyl)amine and 54 g. Na2CO3 in 450 g. H2O at 70°, heating 1 hr. at 95°, cooling, and extracting with Et2O. Reaction of 450 g. I and 690 g. SOCl2 at 125° 1 hr., yielded N-(4-tolylsulfonyl)-N-(β-chloroethyl)-N-(β-chloropropyl)amine (II). Adding slowly 9.3 g. aniline in 15 cc. cyclohexanol to a hot mixture of 31 g. II, 32 g. Na2CO3, 0.1 g. KI, and 215 g. cyclohexanol, refluxing 48 hrs., cooling, filtering, adding C6H6, Et2O, H2O, and concentrated HCl precipitated 1-(4-tolylsulfonyl)-3-methyl-4-phenylpiperazine-HCl (III), m. 214-20° (decomposition). Powdered 3-methyl-4-phenylpiperazine-2HBr, m. 193.4-9° (decomposition), was prepared by stirring at 30° 24 hrs. 93.5 g. III, 71.7 g. phenol, and 570 g. 30% HBr in AcOH, treating the product with Et2O, then boiling acetone. The free base in 4-methyl-2-pentanone was refluxed 22 hrs. with 11.2 g. γ-chloro-4-fluorobutyrophenone, 12.7 g. Na2CO3, and 0.1 g. KI; the product was treated with active C, then with dry HCl in Et2O to yield 1-[γ-(4-fluorobenzoyl)propyl]-3-methyl-4-phenylpiperazine-2HCl, m. 227-34.5° (decomposition). Following 1-substituted-3-methyl-4-substituted-piperazines were similarly prepared (1- and 4-substituents and m.p. given): γ-benzoylpropyl, Ph (di-HCl salt), 229-33° [4-(2-anisyl) analog (di-HCl salt) m. 212-15°]; γ-(4-anisoyl)propyl, Ph, 92-3.8° [4-(2-anisyl) analog (di-HCl salt) m. 199-200°]; γ-(2-thenoyl)propyl, Ph (di-HCl salt), 214-15.5° [4-(2-anisyl) analog (di-HCl salt) m. 213-14.5°]; γ-(4-fluorobenzoyl)propyl, 2-anisyl (di-HCl salt), 212-13°. 1-[γ-(4-Anisoyl)propyl]-4-phenylpiperazine, m. 85-6.2°, was obtained by adding dropwise 180.9 g. 1-phenyl-4-(cyanopropyl)piperazine in 700 cc. Et2O to a stirred solution of 211 g. 4-anisylmagnesium bromide in 700 cc. Et2O, refluxing 1 hr., treating with dilute HCl, heating gently the aqueous solution 1 hr., and extracting the alkalized solution with CHCl3.

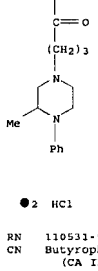
IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl- 102758-21-4P, Butyrophenone, 4'-methoxy-4-(3-methyl-4-phenyl-1-piperazinyl)-108983-89-7P, 1-Butanone, 4-(3-methyl-4-phenyl-1-piperazinyl)-1-(2-thienyl)-, dihydrochloride 110531-91-4P, Butyrophenone, 4-(3-methyl-4-phenyl-1-piperazinyl)-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 102758-21-4 CAPLUS
CN Butyrophenone, 4'-methoxy-4-(3-methyl-4-phenyl-1-piperazinyl)- (6CI) (CA INDEX NAME)

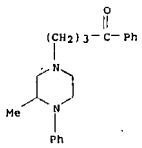


RN 108983-89-7 CAPLUS
CN 1-Butanone, 4-(3-methyl-4-phenyl-1-piperazinyl)-1-(2-thienyl)-, dihydrochloride (6CI) (CA INDEX NAME)



●2 HCl

RN 110531-91-4 CAPLUS
CN Butyrophenone, 4-(3-methyl-4-phenyl-1-piperazinyl)-, dihydrochloride (6CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 134 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:36037 CAPLUS
DOCUMENT NUMBER: 49:36037
ORIGINAL REFERENCE NO.: 49:6967e-i,6968a-b
TITLE: Derivatives of piperazine. XXIV. Synthesis of 1-arylpiperazines and amino alcohol derivatives
AUTHOR(S): Pollard, C. B.; Wicker, Thomas H., Jr.
CORPORATE SOURCE: Univ. of Florida, Gainesville
SOURCE: Journal of the American Chemical Society (1954), 76, 1853-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

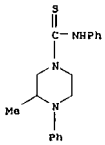
AB cf. C.A. 48, 7616a. A series of 8 1-arylpiperazines (I) have been prepared by the reaction of mixed HCl salts of aromatic amines and diethanolamines. Derivs. of the I were prepared by the reaction with ethylene oxide (II), 3-methoxypropylene oxide (III), Ac2O, BzCl, and PhNCS. p-ClC6H4NH2 (280.6 g.) and 210.3 g. (HOCH2CH2)2NH carefully neutralized with 375 cc. 37% HCl (d. 1.19), the mixture heated with continuous removal of the H2O, neutralized with 180 g. NaOH in 300 cc. H2O, and the resulting oily layer distilled gave 205 g. (52.3%) 1-(4-chlorophenyl)piperazine (IV), b5 155.7-7.2°, m. 71.5-3.5°. Similarly were prepared the following I [1-aryl and other substituents if present, % yield, b.p./mm., d20, and nD25 given]: p-MeC6H4 (V), 25.5, 150.9-2.5°/10, -, -; m-MeC6H4 (VI), 22.8, 154.2-6.2°/10, 1.0383, 1.5744; o-MeC6H4 (VII), 26.5, 136.5-7.5°/10, 1.0261, 1.5600; m-ClC6H4 (VIII), 38.4, 157.2-8.2°/5, 1.1897, 1.5985; o-ClC6H4 (IX), 32.7, 133.9-4.9°/5, 1.1763, 1.5794; 1-Ph, 2-Me (X), 30.7, 138.5-40.5°/10, 1.0410, 1.5723; 1-Ph, 3-Et (XI), 20.3, 147.8-9.8°/10, 1.0327, 1.5635. IV shaken with a slight excess of BzCl in the presence of excess 10% aqueous NaOH and the product recrystd. from EtOH gave the 4-Bz derivative of IV, m. 128.0-9.5°. Similarly were prepared the 4-Bz derivs. (m.p. given) of: V.HCl, 201.6-3.6°; VI.HCl, 202.6-4.6° (decomposition); VII, 122.5-3.5° VIII.HCl, 158.3-9.8°; IX, 130.5-32°. IV refluxed 0.5 hr. with a 4-fold excess of Ac2O, the mixture poured into 100 cc. ice water, neutralized with solid Na2CO3, and the product recrystd. from EtOH gave the 4-Ac derivative of IV, m. 99.5-101.5°. Similarly were prepared the 4-Ac derivs. (m.p. given) of: V, 109.5-10.5° (from H2O); VI, 46.7-8.2°; VII, 55.9-7.9° VIII, 42.2-4.2°; IX, 65.5-6°; X, 57.4-9.4°; all derivs. (except that of V) separated

as oils and were dissolved in Et2O, dried with K2CO3, and the residue from the Et2O solution recrystd. from heptane. IV (19.66 g.) in 100 cc. MeOH treated during 15 min. with 8.8 g. III, the mixture refluxed 3 hrs., the MeOH removed in vacuo, the residue cooled, and the resulting solid recrystd. from heptune yielded 13.5 g. (47.5%) 1-(4-chlorophenyl)-4-(2-hydroxy-3-methoxypropyl)piperazine, m. 78-9.5°. Similarly were prepared the 4-(2-hydroxy-3-methoxypropyl) derivs. (% yield and m.p. given) of: V, 61, 77.5-79°; VI, 44.6, 56.5-7.5°; VII, 46.7, 38-9°; VIII, 34.4, 58.8-9.8°; IX, 70.4, 90-1.5°; X, 56, -, b0.3 151.5-3.5°. II (4.405 g.) introduced near the bottom of a solution of 19.66 g. IV in 100 cc. MeOH at such a rate as to avoid boiling, the mixture stirred several hrs. at room temperature, the MeOH evaporated on the steam bath, and the residue cooled and recrystd. from heptane gave 19.5 g. (81.2%) 1-(4-chlorophernyl).4-(2-hydroxyethyl)piperazine, m. 107-8.5°. Similarly were prepared the 4-(2-hydroxycthyl) derivs. (% yield and m.p. or b.p./mm, given) of: V, 35.5, 51.5-2.5°; VI, 31.8, 67-8.5°; VII, 65.6, 146-9°/1.5 (di-HCl salt, m. 175.1-6.6°); VIII, 33, 97.5-8.6°; IX, 55, 166-9°/2.3 (mono-HCl salt, m. 154.2-5.7°); X, 74, 167-72°/1 (di-HCl salt, m. 235.2-6.5°); XI, 67, 156-8.2°/2.2.

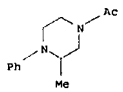
IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl- 4318-46-1P, 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio- 856839-29-7P, Piperazine, 4-acetyl-2-methyl-1-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 4318-46-1 CAPLUS
CN 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio- (7CI, 8CI) (CA INDEX NAME)



RN 856839-29-7 CAPLUS
CN Piperazine, 4-acetyl-2-methyl-1-phenyl- (5CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 15:47:08 ON 18 SEP 2007)

FILE 'REGISTRY' ENTERED AT 15:47:13 ON 18 SEP 2007
L1 STRUCTURE UPLOADED
L2 0 S L1 FULL

FILE 'REGISTRY' ENTERED AT 16:01:11 ON 18 SEP 2007
L3 STRUCTURE UPLOADED
L4 4 S L3 FULL

FILE 'CAPLUS' ENTERED AT 16:01:46 ON 18 SEP 2007
L5 1 S L4 FULL

FILE 'REGISTRY' ENTERED AT 16:07:59 ON 18 SEP 2007
L6 STRUCTURE UPLOADED
L7 1347 S L6 FULL

FILE 'CAPLUS' ENTERED AT 16:08:40 ON 18 SEP 2007
L8 201 S L7 FULL
L9 134 S L8 AND PY<2003